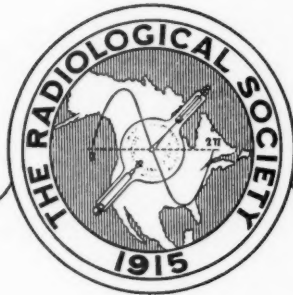


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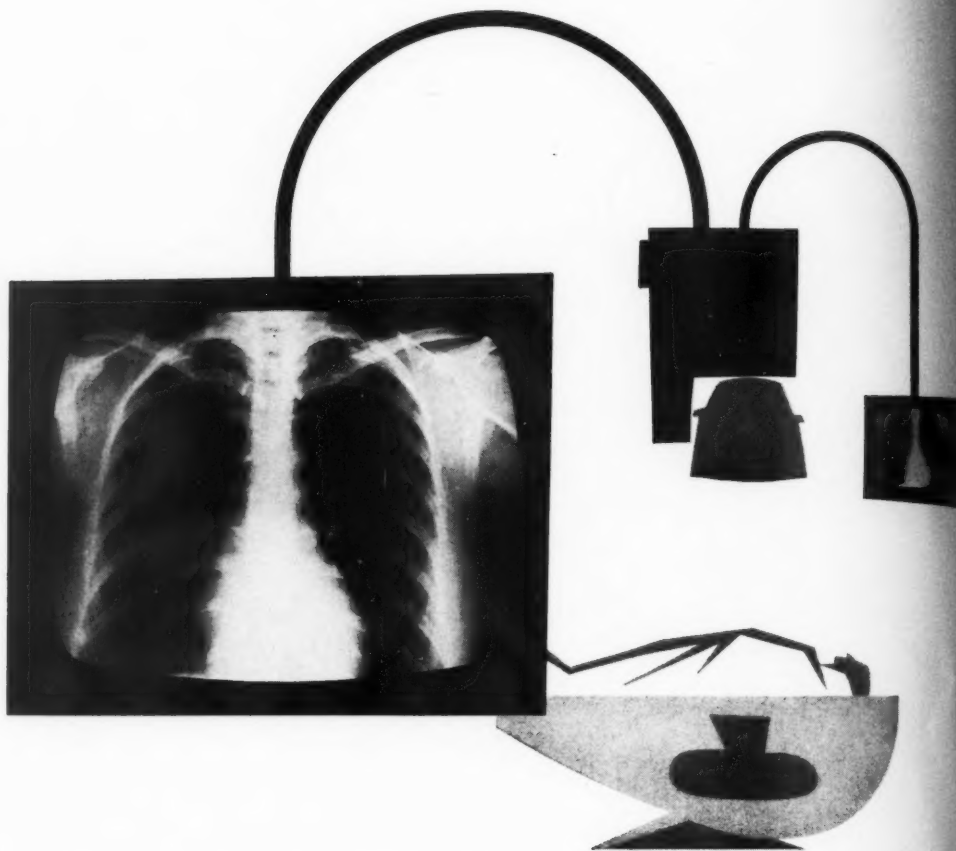
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RADIOLOGY

A MONTHLY PUBLICATION DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES

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No. 4

Introduction of the Memorial Fund Lecturer Payne S. Harris, M.D.

LEO G. RIGLER, M.D.

IT IS MY privilege to present the Memorial Fund Lecturer. This lectureship was established in 1955 through the wise efforts of Dr. Walter Wasson and his colleagues on the Board of Trustees of the Society at that time, as an award of distinction for a young man who has done outstanding research in radiology or related scientific discipline. I might say parenthetically that, as members of the Board of Trustees get older, it becomes more and more difficult to define and delimit this term, "young" man.

Since the first Lecture in 1956, these distinguished addresses have taken on a specific and rather unique character, for the Memorial Fund Lectures have carried us forward into relatively unexplored areas and have opened up for us new scientific vistas, widening the horizons of our knowledge and giving us glimpses of potential developments which have been enormously stimulating.

It seems particularly fitting, therefore, that our lecture today should send us soaring off into outer space. We are to hear from one of those amazing scientists who is both a physicist and a physician, whose whole career has been devoted to the exploration of the outer fringes of knowledge in the realms of radiation.

Dr. Payne S. Harris took his first degree in physics at the University of

Illinois and was graduated from the medical school of that University in 1946. Entering the Army after his internship, he has been in the service of our defense forces in various capacities ever since. He worked on the design and construction of the third betatron, and since 1948 he has concerned himself largely with nuclear weapons at Los Alamos, where he is now an alternate leader of the Health Research Group.

He has traveled all over the world in search of knowledge, and in his capacity as consultant to the Surgeons-General of the Army and the Air Force. His research has been varied, his interests broad, and his intellect (I am told by his colleagues) almost overwhelming. Dr. Harris is one of those remarkable people who can talk intelligently and authoritatively with weapons designers on the one hand and with radiation biologists on the other. His association with the nuclear rocket program and his own research suggest that he is perhaps one of the best informed men in this country on the subject he is to discuss.

Members of the Radiological Society of North America are fortunate to have the opportunity of hearing Dr. Payne S. Harris whose address is entitled "Radiation in Outer Space: Natural and Man-Made."

Space Radiations: Natural and Man-Made

Memorial Fund Lecture¹

PAYNE S. HARRIS, M.D.

THROUGHOUT THE history of man, his advancement has been colored by his environment. No advance, technological or otherwise, has been possible unless man himself has been able either to adapt to or control his surroundings.

The past fifteen years have seen tremendous strides in the application of nuclear energy from destruction to construction. The primary limitation to continued advance lies in the radiation environment of this energy source and its possible untoward effects on the health of man.

Man is on the threshold of another scientific adventure—the entry into space. Here again the question of the environmental limits to progress has arisen. In this new area of effort, radiation appears to be of primary concern. Since radiation exists as one of the hostile perimeters of space, and since nuclear energy with its concomitant radiation may be necessary for significant advance in space conquest, it appears only reasonable to review our knowledge of the field.

PHYSICAL AND BIOLOGICAL CONCEPTS OF NATURALLY OCCURRING SPACE RADIATIONS

Cosmic Rays: The presence of cosmic rays has been known for many years. The majority of the measurements which have contributed to our knowledge have been made within the atmosphere and up to its top.

The physical nature of cosmic rays is reasonably familiar. The primary cosmic-ray beam apparently originates in interstellar space and it will, therefore, be with us in any travels, whether in this galaxy or others. The primary component is found to consist of 79 per cent protons, 20 per cent alpha particles (He nuclei), 0.78

per cent carbon, oxygen, and nitrogen nuclei, and 0.22 per cent nuclei of atomic number greater than 10. The kinetic energies of these particles are found to vary from one to several billion electron volts (Bev) per nucleon. Thus, an iron nucleus with an atomic number of 56 and an energy of 10 Bev per nucleon would have a total energy of 560 Bev. When the primary cosmic ray interacts with an interposed material, such as the "skin" of a spaceship or our atmosphere, secondaries are produced. These depend upon the interposed material but would generally consist of particles of lower atomic number than the primary—electrons, mesons, gamma rays, and neutrons.

The cosmic-ray intensity varies with respect to the observer's relation to the earth's geomagnetic field and with respect to solar flare incidence. Over long periods, however, at any particular position with respect to the magnetic field the average intensity is fairly constant. Thus, it is reasonable to estimate the average cosmic-ray dose rate. In "free" space (away from the shielding effect of the earth), the cosmic-ray dose rate approximates 25 mrad per day. The presence of a spaceship "skin" and other materials might tend to increase this ionization figure by a factor of as much as 4. It is apparent that rates of this order are entirely acceptable if the biological effects are not enhanced by the particles themselves.

The medical problems associated with cosmic rays thus stem from their particulate nature and the interaction probabilities in tissue. The obvious differences in the transfer of energy to tissue by cosmic rays as opposed to the x-rays, gamma rays, and electrons of conventional experience are two: the production of stars, and the

¹ From the Los Alamos Scientific Laboratory, University of California, Los Alamos, N. Mex. Presented at the Forty-sixth Annual Meeting of the Radiological Society of North America, Cincinnati, Ohio, Dec. 4-9, 1960.

dense ionization of heavy charged particles. Star production (inelastic collision with a nucleus) results in degradation of the striking nucleus to several smaller nuclei, with resultant partition of the available kinetic energy. These smaller nuclei then lose energy through ionization until stopped. Ionizing heavy nuclei produce a continuous ionization track, becoming more dense toward the end until stopped. It is apparent that, at the point where a star is produced, cellular or molecular death will occur. It is also apparent that death will take place in a densely ionized track (where the core dose may approximate several thousand rads).

It is difficult, however, to assess the overall effect of such transitions. Some postulations may be made. In the first place, in tissue the probability of star formation exceeds the probability of a heavy particle spending all its energy on ionization. Thus, the overall effect is lessened, since the ionization track of the star secondary has neither the density nor length of the primary. Second, the greater part of the lifetime of a charged particle in tissue is spent in getting rid of its energy at the same rate as more conventional radiations such as x-rays and neutrons. Since these radiations are not particularly efficient in producing damage, there is no reason why heavy charged particles should be so. Third, it appears that the efficiency of radiation in producing damage goes through a maximum and then falls, no matter what the end-point effect. Roughly, the efficiency is related to the rate of energy loss or to the lineal energy transfer in the biological system. This would imply that, although cellular death would certainly occur in the center of the column of dense ionization by heavy particles, a large proportion of the energy deposited is wasted and surrounding cells retain their repair or compensating properties.

Certainly, the ability of undamaged cells to repair or compensate for radiation-killed cells is important. In a system

as complex and at the same time as "disordered" as that of man, the overall effect of a columnar volume of killed tissue may be of little or no consequence. Although the redundancy of all tissues is unknown, it appears that the available fluxes and interaction probabilities of cosmic rays are not sufficient to cause serious damage, and their efficiency in producing injurious effects in man may be less than 1 when compared with conventional radiations.

Geomagnetically Trapped Corpuscular Radiations: In 1958, the presence of high-energy radiation above the atmosphere with intensities greatly exceeding that of cosmic rays was discovered by Van Allen and his colleagues. Subsequent studies have resulted in remarkable strides in identifying this radiation and its cause. Apparently the radiation consists of particles trapped in the earth's geomagnetic field—primarily protons and electrons. One prime source may be neutrons escaping the earth's atmosphere after production from cosmic-ray interaction in the upper atmosphere and subsequent decay into protons and electrons. A second source may be electron streams from cataclysmic events on the sun. The radiation shells thus produced are divided into two layers called the inner and outer Van Allen belts.

The inner Van Allen belt consists of protons with energies up to 700 Mev and electrons with a maximum energy of about 800 kev. The energy spectrum of the protons can be represented by the power function $N_0 E^{-K}$, when E is energy and $K = 1.5$. Thus, the average energy is about 120 Mev. The electron spectrum appears to be a degraded beta-ray spectrum with the aforementioned maximum energy. The belt begins at an altitude of about 1,000 km. and extends outward, reaching an intensity maximum at about 3,000 km. Its intensity is stable with time. It surrounds the earth except in the polar regions (latitudes less than 20°) and thus has a shape that can be compared to a doughnut.

The maximum surface dose rate from the proton component of the inner belt has been estimated to be about 100 rads per hour. On the basis of the proton spectrum and the probability of energy loss in tissue through ionization, the depth dose may be estimated. For instance, at the center of the body (assuming isotropically distributed protons and no external shielding) the dose rate would be about 100 mrad per hour under these intensity conditions and would be contributed to only by protons of energies greater than 150 Mev. These estimates do not take into account star formation or spallation by high-energy protons. Shielding may also play an important part in reducing the ionization dose rate. For instance, a shield of low Z -number material equivalent to the human skull (0.75 gm./cm.^2) would reduce the rate to about 1 rad per hour immediately below the shield. Also, the damaging efficiency of these protons is not absolutely known. The specific ionization of the protons above a few Mev in energy, however, approximates that of hard x-rays or electrons of a few hundred kev, and the efficiency may therefore be assumed not to exceed 1.

The electrons of the inner Van Allen belt are analogous to those found in the beta-ray spectra of a variety of common radioisotopes. As such, the unshielded surface dose rates may be high, corresponding to multicurie isotope sources. These may be reasonably shielded, however. The most important medical aspect of these electrons is the production of bremsstrahlung in the shield. As an example, consider a thin metallic spaceship "skin" such as stainless steel. In the inner Van Allen belt, the peak electron flux (with energies up to 800 kev) may run as high as $2 \times 10^{10}/\text{cm.}^2/\text{sec.}$ For a spherical ship with a radius of 2 meters, the incident integral surface flux is about 10^{16} electrons/sec. This is equivalent to a "current" of about 1.5 milliamperes, and the spaceship thus becomes the target of an x-ray machine operated at an average of a

few hundred kev and a current of 1.5 ma. By the judicious use of low Z materials with high Z liners, the electrons and bremsstrahlung may both be minimized.

The outer Van Allen belt has been found to consist primarily of low-energy electrons similar to the auroral radiation. It is much greater in extent and depth than the inner belt, beginning at about 12,000 km. and decreasing in intensity far out in space. It is also roughly doughnut-shaped but its latitudinal margins are limited ($<50^\circ$) in comparison with the inner belt. The intensities found within the outer belt vary quite widely, and the limits of variation are related to solar flares. The electron spectrum is softer than that of the inner belt, extending upward to only a few hundred kev, but the fluxes are higher. Fluxes of the order of $10^{11}/\text{cm.}^2/\text{sec.}$ for energies greater than 20 kev and of $10^8/\text{cm.}^2/\text{sec.}$ for energies greater than 200 kev have been noted. The latter could give surface dose rates of the order of 10^4 rads per hour. Such rates seem extremely high but, as previously noted, the judicious application of shielding would reduce the rate to a negligible value.

Solar Flare Radiations: Solar flare radiations, as the name implies, are related to sunspot production. They may be connected with rapidly varying sunspot magnetic fields. The visual phase lasts only a few hours, but the radiations themselves may continue for a matter of days. In this case, the radiations of interest are again protons and electrons. The proton spectrum is much steeper than that of the inner Van Allen layer, but the energies may extend into the Bev range. The intensities may attain values above the cosmic-ray levels. Also, flare phenomena may sharply increase the observed intensities in the outer Van Allen belt. For the more frequent solar disturbances, dose rates of protons with energies above 25 Mev may exceed 35 rads per hour for a number of days. For a rare giant solar flare, such as that

of Feb. 23, 1956, the rate may be of an order of magnitude above that noted. Since these events are unusual, it appears reasonable to accept the situation as a calculated risk and make plans with the more usual occurrence in mind. The medical consequences of such phenomena may be related directly to the previous discussions of high-energy charged particles.

PHYSICAL CONCEPTS OF MAN-MADE SPACE RADIATIONS

As man extends his frontiers of knowledge into the environment of space, the utilization of nuclear energy in space appears to be of great importance. It is, therefore, only reasonable to look into the future and make some estimates of the uses of nuclear energy and their effects in this new environment.

Several systems for the utilization of nuclear power in space have been proposed, some of which are being actively pursued. These systems include nuclear reactor rocket propulsion, nuclear auxiliary power systems for space use, and atomic explosions for space propulsion. Also, there are proposals for the use of space as a proving ground for scientific experiments and proof tests using nuclear explosives. All of these systems may in one way or another modify the radiation environment of space, and thus have medical implications as far as manned space operations are concerned. In addition, as a consequence of their use, there may also be related effects on the public domain on earth.

Nuclear Reactor Propulsion for Rockets: In the past two years, progress has been made in the use of nuclear reactors as a propulsion source for rockets. The advantages of such a propulsion system over chemical systems lie in the greater payloads per total rocket weight that may be lifted into orbit or into escape profiles. The radiation problems associated with such a power source arise with projected use of such systems.

The physical concepts of reactor sources

used in this manner include high powers (multimegawatts) acting for short times (minutes) to heat propellant gases to high temperatures. Thus, the radiation problems that must be considered (even in the case of normal operations, as well as in accident situations) include the gamma and neutron source strength during operation, the leakage of fission products or activated materials into the propellant gas stream, and the residual activity of the source after shutdown.

Estimates may be made of the magnitude of the radiation source terms for nuclear reactor rocket propulsion systems. A possible useful system has been estimated to produce 3×10^5 megawatt-seconds of power. To compare with other nuclear power sources, this value can be equated to 70 tons of high explosive energy or to 0.07 kiloton equivalent yield. Similarly, such a system would produce the same total radioactivity during its operational period as a small 1-megawatt power reactor would give in about four days of continuous operation. It can be seen that these are relatively small numbers in comparison to nuclear explosives and static power sources.

In the frame of use of these systems, the source strength cannot be neglected, however. It is apparent that, for economy of weight, protective shielding must be minimized. One is dealing, therefore, with an essentially bare source. For neutron dose estimation, a leakage from the source of 1 neutron per fission can be assumed. Since 1 megawatt-second produces 3.3×10^{16} fissions, the total neutron source strength is 10^{22} . This could give significant neutron fluxes and doses at various distances, depending on the amount of air absorber between the source and the receiver. Similarly, such a source during operation at its rated power would be a gamma source of some hundreds of megacuries equivalent. At a dose rate of 1 r per hour for 1 curie at 1 meter, significant gamma doses could be delivered at rather large distances.

As noted previously, fission products

can be expected to leak into the propellant gas stream even under normal operating conditions. The constitution and magnitude of this contamination are dependent upon design and operating parameters. To get an idea of magnitude, we may assume that all of the strontium and its precursors produced during operation leaked out. Thus, there would be produced a column of strontium activity over the atmospheric and spatial limits of the operating phase which, in total, would be the same as that produced by a 70-ton nuclear weapon detonated in air, and this could enter the biospheric inventory at the same rates as weapon fall-out, depending on the location of the fall-out at time of production.

The residual radioactivity remaining after shutdown will constitute a multi-megacurie source of gamma rays. The intensity of this source with time will follow the laws of fission product decay and therefore constitutes a problem depending upon time after shutdown and the environment in which the source happens to be located.

If an accident involving one of these systems does occur, the magnitude may be reasonably estimated. The most serious accident that might be envisioned would be the induction of prompt criticality in the reactor by suddenly increasing, in some way, the reactivity of the system. With the model assumed initially, the maximum effect that could be produced would be only 3 per cent of the total energy production during a normal operational run. There would be no explosion, as such, although vaporization of a portion of the reactor core would take place and at least partial disassembly might occur.

Space Nuclear Auxiliary Power Units: A new and exciting tool for use in space investigation is nuclear power as a source of electrical energy. Two types of system have been built or are under study. These are thermoelectric power units in which radioactive isotopes or small reactors constitute the power source.

Isotope units utilize multimegacurie

amounts of alpha or beta emitters to produce power. The radioactivity is absorbed in various materials. This increases the temperature of the absorber. The temperature change causes current flow in thermocouples imbedded in the absorber. The current produced is a source of electrical energy of a few watts, which is available for use with the payload. The small package reactor unit operates at some nominal level and produces by some heat transfer or direct transfer system a few kilowatts of electrical power for similar payload use.

The useful source strengths of isotope units depend on the isotope and its decay scheme. Polonium 210, an alpha emitter, has been utilized. From this nuclide satisfactory power may be developed with a few thousand curies. Cerium 144, a beta-gamma emitter, has also been suggested; satisfactory power can be developed with a few tens of thousands of curies of this material. Thus, in any medical considerations the interest lies in containment of kilocurie amounts of material, shielding in the case of mixed gamma sources, and spread of the material in the event of accident.

For package reactor electric power units, the level of operation is in the kilowatt region. It can be assumed that reactors used for payload power would not be operated, and thus could be considered "cold," until the payload is established in its position in space. Thus, the initial medical problem would involve possible spread of nuclear fuel in case of accident. In space, the operating time of such a power system might approach a few years. If operation is assumed to be at a power of 100 kilowatts, the source strength at any time would be much less than for a rocket propulsion reactor. The total fission product inventory for the longer half-lived nuclides, however, would far outstrip that of the propulsion reactor. For instance, for Sr^{90} and Cs^{137} , an operational period of about one month would produce an inventory equal to that of the propulsion reactor during its entire

operating period. Medical considerations would therefore involve the reactor source in space and the dispersion and decay of the source after shutdown, orbital de-generation, re-entry, and the like.

Nuclear Explosion Propulsion Systems: It has been suggested that, in order to project very large payloads into space, nuclear explosions be used as sources of energy. It is obvious that an extremely large amount of energy per pound of fuel is available from nuclear explosions, and the payoff in ratio of payload weight to fuel weight is certainly appreciable. Initial studies certainly indicate that this method of producing thrust may be feasible.

The problems associated with such a system are apparent. In this case, at least kilotons of energy are being released into the air and into space in almost exactly the same manner as with air-burst nuclear weapons. Thus, there are the problems of radiation, blast, and thermal protection close to the source, and the whole problem of fall-out from the atmosphere and from space. To get an idea of the magnitudes involved in this system, it would appear reasonable that a few hundred kilotons of energy released fractionally throughout the course could be used to lift a large payload into some particular orbit. A single event of this type can be compared with the release of several megatons per year in a nuclear weapon-testing program.

SPACE AS A PROVING GROUND AND EXPERIMENTAL AREA

Space has been suggested as a testing ground for nuclear explosions and as a scientific study area for natural phenomena which could require nuclear detonations as part of the experimental design. The nuclear detonations used in the study of the *Argus effect* are an example of the latter application. In this case, the entrapment of electrons (from beta-ray-emitting fission products) in the earth's geomagnetic field was studied. Nuclear detonations of a variety of magnitudes have been suggested for use in investigations of fundamental

geophysics from a spatial arena. Proof testing of nuclear weapons in a space testing ground is an ideal means of eliminating certain of the atmospheric testing problems which plague us continuously. The fall-out problem, for instance, could be practically eliminated. Space contamination and disturbance of the normal radiation environment of space, however, could become a headache at some future time.

Again, the primary medical problems would involve the total energy release of the test, post-explosion contamination, and possible accidental detonation after abort, etc.

THE MEDICAL PROBLEMS OF MAN-MADE SPACE RADIATIONS

The physical concepts of the various applications of nuclear energy in the space environment have been introduced in the previous section. For medical considerations, it appears reasonable to break down the systems into areas of effect. A convenient breakdown is through separate consideration of effects on personnel intimately concerned with the system operation and effects on the public domain. To get an idea of magnitudes, normal operations as well as accidents may be considered.

The medical effects of normal operations of these systems or of accidents that may occur during their use may be classified by the phase of operations in which the event takes place. These operational phases include ground testing and check-out prior to the launch; the period from the launch until orbital achievement or test point in space; the orbital phase; and the phase of re-entry and impact.

During ground test, the radiation problem would be of primary concern only in the case of nuclear reactor rocket propulsion. It is improbable that propulsion by nuclear detonations would be ground-tested with live nuclear sources. Similarly, in systems where the radiation source is only carried by a vehicle, ground test would constitute a check-out of the

vehicle itself. In the ground-test phase of a rocket reactor propulsion system, consideration must be given to the source strength, leakage into the propellant gas stream, residual source strength after shutdown, and accidental excursion during this phase. Referring to a nominal system mentioned previously, the source strength would be that of a 3×10^6 megawatt-second source. The dose at 1 mile would be about 60 mrad, while at 10 miles it would be essentially zero. The dose due to cloud contamination by material leaking into the gas stream during normal operation would amount to a few hundred millirads at distances of the order of 1 mile. As noted previously, the maximum accident which might be expected in this case would result in a fission yield of about 3 per cent of the above integrated power and a release of some 15 per cent of the core. If such an accident is superimposed on a full period of reactor operation, the total dose, including source strength, cloud passage, and residual contamination, is of the order of 2 rads at 1 mile and 140 mrad at 10 miles.

During the prelaunch check-out and at launch, failure might occur in any of the systems, with an accident involving the nuclear source. Nuclear yield with resultant contamination would be expected to occur only in the case of a first- or second-stage nuclear rocket reactor or in a nuclear explosion propulsion system. A thermoelectric isotope unit would be packaged, necessary for containment, while a reactor unit would be "cold" and, although it might be broken up with local scatter of fuel, it would be "safed" for nuclear yield. Nuclear detonants carried for space testing or scientific experiments would also be "safed," with the probability of nuclear yield of any amount approaching zero. The nuclear rocket reactor first-stage system would give source and contamination results as above, increased by the power inventory accumulated prior to accidental excursion. The minimum would occur if the reactor were "cold" and was to be used as a second

stage only. Here, the accident-only doses may be estimated at 80 mrad at 1 mile and 10 mrad at 10 miles.

It is obvious that the system involving nuclear detonations for propulsion is in a category by itself. Here the dose estimations may be considered in the usual manner of all nuclear detonations and will be a function of yield. It need only be pointed out that the yields per explosion will be of the order of kilotons.

In operations in the period post-launch to orbital or test-point achievement, the main medical concern is fall-out in any system used. Normally there would be fall-out only from the propulsion systems. In case of accident, fall-out from isotope units might be considered if breakup occurred. If our nominal rocket reactor were assumed to release all of its fission products in the troposphere and lower stratosphere, 250 of these could be operated before the contribution to biospheric contamination would reach that from a nominal 20-kiloton bomb. In addition, a first-stage system would spend only about one hundred seconds of its operating history in a region where the return time of fission products is short. Above a few hundred thousand feet, the return time may be in excess of one hundred years. It is estimated that 10,000 tests per year of this nominal reactor could be conducted without increasing the present biospheric level of strontium 90 and cesium 137.

Although the probability of isotope release is small in thermoelectric applications, it should be considered. Assuming an isotope unit containing about 2,000 curies of polonium 210, the surface fall-out concentration on dispersal from the lower stratosphere would be about 10^{-6} times the soil concentration of $6.5 \mu\text{mc}/\text{gram}$ for the naturally present isotope. Similarly, the air concentration from the fall-out situation would be only about 3×10^{-4} times the normal natural air concentration of the nuclide, which has been estimated to contribute to about one-third of the normal ground concentration.

The fall-out from an explosion-propul-

sion source would be by far the largest contributor of any of these systems. This component might be equivalent to several tens of kilotons per launch before the vehicle was far enough in space to lengthen the return time of the fission product contaminants to inconsequential values.

In orbiting systems, the medical problems involve only local protection in the case of manned systems. Here distance and shielding may be used ideally to minimize the radiation in the case of a shutdown nuclear rocket engine or from an operating thermoelectric power source. For tests or scientific experiments involving nuclear detonations, the main problems involve contamination of space itself and, because of the special consequences of the environment (the presence of a vacuum, change in gravity, etc.), some question of the range of effect of these sources.

Failure of orbital achievement and orbital decay both bring up questions involved in re-entry. If system burn-up occurs on re-entry, the spread of contamination will be controlled by the point of burn-up. Since this is above the stratosphere, the return time of contaminants to earth will be restricted to orders of one hundred years or greater. The level of contamination will depend on the operating time, on the system, and on the interval between shutdown and burn-up. In nuclear rocket reactor propulsion, a full inventory of fission products decreased by decay post-shutdown will be available. Thermoelectric isotope sources

will always be of less activity than at launch. Reactors used for electric power will build up fission product activity only after orbital achievement.

If burn-up on re-entry does not occur, the local effects of impact must be taken into account. As an example, we may consider the source strength of the nominal nuclear propulsion reactor after shutdown. At 10 meters from the source, the dose rate is about 1,000 r per hour at one day. At one year, the rate is about 10 r per hour. The doses from a 100-kilowatt reactor electric power source would approximate these same values after a month or so of operation with the same shutdown periods as noted here.

SUMMARY

A general review of the physical and medical concepts of space radiations, their sources and effects is presented. It is apparent that many problems are involved covering the radiation source and effect spectrum as it is known today, and that a thorough understanding of the problems affecting man may be paramount in his scientific advance into the spatial environment. The standards of protection and the level of risk that are acceptable for space exploration must be established in the light of this and subsequent studies if the full potential of man is to be realized in space conquest.

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(Pro le summario in interlingua, vider le pagina sequente)

SUMMARIO IN INTERLINGUA

Radiation de Ambiente: De Origine Natural e Human. Conferentia de Fundo Memorial

Un revista general del conceptos physic e medical del radiationes de ambiente—de lor origines e lor effectos—es presentate. Radiationes ambiental de origine natural es debite a radios cosmic, a geomagneticamente trappate radiationes corpuscular, e a radiation de eruptiones solar. Radiationes ambiental de origine human include le radiation ab reactores nucleari usate in le propulsion de rochettas, generatores nucleari de energia auxiliar, e systemas de propulsion per explosiones nucleari.

Le fontes de radiation ambiental que es de origine human pote esser manipulate quantitativemente in le milieu astronomic como illos esserea manipulate sub conditiones terrestre, con le supposition que le coefficients de attenuation approcharea zero. Rochettas nucleari va disseminar un portion de lor fonte de fortia al longo de lor curso combustive e plantar assi un active fonte de radios gamma e de electrones post lor strangulation o exhaustion. Generatores auxiliar de fortia nucleari constitueran fontes-puncto de radios gamma

e de neutrones de varie nivello de potentia durante le tempore de lor activitate. Systemas de propulsion in bombas esserea transiente in lor rendimento de alte intensitate e resultarea in un forte contamination de spatios local con fontes de radios gamma e beta. Ab le puncto de vista medical, le effectos in le personal directemente concernite con le operation del systema debe esser separate ab le effectos in le dominio public. Le processos normal e etiam le occurrentia de accidentes es prendite in consideration.

Es apparente que multe problemas inherere in le question del fontes de radiation e del spectro de effectos de radiation e que un precise comprehension de ille problemas in tanto que illos affice le homine va esser requirite como base de nostre progresso ad in le milieu del spatio cosmic. Il va esser necessari establir standards de protection e de riscos acceptabile in le exploration del spatio extraterrestre si le complete potentialitates del homine in su conquesta de ille spatio debe esser realisate.



Roentgen Evaluation of Pulmonary Arterial Pressure in Mitral Stenosis¹

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QUANTITATION OF pulmonary hypertension in mitral stenosis is of clinical importance not only for determination of the severity of the mitral block but also for prediction of the reduction in pressure to be expected after valvulotomy. The demonstration of resting obstructive pulmonary hypertension, therefore, has become established as a major indication for surgical treatment in this form of rheumatic heart disease. If a main purpose of cardiac catheterization in mitral stenosis is the mensuration of pulmonary arterial pressure, then an accurate roentgenologic method for prediction of that pressure would be of significant clinical value. It is the purpose of this paper to review attempts made in the past to relate roentgen findings to pulmonary arterial pressure and to report the value of newly devised multi-parameter formulas for that purpose.

PRIOR INVESTIGATION

Presence of Kerley's B-Lines: Twenty-seven years ago Kerley (11) stated, with respect to the chest roentgenogram in mitral stenosis, that after "a severe attack of passive hyperaemia . . . the shadows of the perivascular lymphatics persist as fine sharp lines, most marked at the bases and near the hila." "Kerley's lines" consist of A-lines, or radiating perihilar lines, and B-lines, or peripheral basal lines. This observation remained relatively unnoticed for many years.

Conditions which result in thickening of the subpleural intralobular septa or dilatation of their lymphatic vessels may produce B-lines. Septal thickening may occur in pneumoconiosis, lymphangitic carcinoma-tosis, hemosiderosis, sarcoidosis, reticulosis, and hilar lymphatic block (Grainger, 9).

Pulmonary venous hypertension of any etiology may produce B-lines. Their occasional presence during left ventricular failure (Short, 18) and chronic passive congestion (Fleischner and Reiner, 7) has been noted. B-lines are rarely if ever seen in uncomplicated pulmonary arterial hypertension (Bruwer *et al.*, 4; Levin, 12).

The development of B-lines in mitral stenosis is presumptive evidence of pulmonary venous hypertension. Attempts to "calibrate" B-lines in terms of coexistent pressures within the pulmonary circulation have shown that the presence or absence of these lines correlates somewhat more closely with the level of pulmonary "capillary" pressure than with mean or diastolic pulmonary arterial pressures (Grainger, 9). There is a range of pulmonary "capillary" pressures above which B-lines are usually seen and below which they rarely appear; this is approximately 20 to 30 mm. Hg (Bruwer *et al.*, 4; Carmichael *et al.*, 5; Fleming and Simon, 8; Grishman *et al.*, 10; Whitaker and Lodge, 19). Rossall and Gunning (14), who measured mean left atrial and pulmonary arterial pressures by transbronchial puncture in 100 patients with mitral stenosis, found that B-lines were never present when the mean left atrial pressure was below 10 mm. Hg. If the mean left atrial pressure was in excess of 24 mm. Hg, B-lines were invariably present.

Width of the Descending Pulmonary Artery: In 1920 Assmann (1) observed that the pulmonary right hilar shadow is narrower in normal persons than in patients with various cardiac diseases. By his measurements, hilar width in normal adult males did not exceed 14 to 15 mm. Wider hili were present in 19 of 20 cases of

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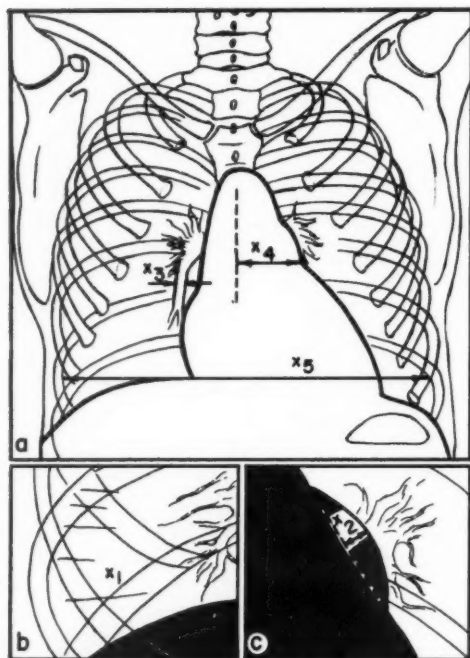


Fig. 1. Roentgen parameters of obstructive pulmonary hypertension used in this investigation. (a) On the erect postero-anterior roentgenogram the width of the right descending pulmonary artery branch (x_3), the "pulmonary artery size" (x_1) and internal thoracic diameter (x_2) were measured. (b) The presence or absence of B-lines (x_1) was determined. (c) The height of the pulmonary artery segment (x_2) was found.

cardiac disease, including mitral valvular disease, but 10 of 37 normal hili were associated with clinically abnormal hearts.

Recently Schwedel *et al.* (16) applied a similar technic to the quantitation of mean resting pulmonary arterial pressure in mitral stenosis by measuring the width of the upper portion of the descending branch of the right pulmonary artery on 2-meter chest roentgenograms (Assmann's roentgenograms were made at 1.5 meters). The vessel is usually well outlined between aerated lung tissue and the air column of the lower lobe bronchus. The investigators concluded that the upper limit of normal width was 14 mm. In all of 68 patients with a vessel width of 15 mm. or more there was significant pulmonary hypertension. However, the correlation between pulmonary arterial pressure and

vessel width was non-linear. Roussel *et al.* (15) also have reported that dilatation of the right descending pulmonary artery branch in mitral stenosis is the most accurate roentgenologic index of pulmonary hypertension.

Other Criteria. Another objective roentgen parameter, which yielded a strong correlation ($r = +0.89$) with mean pulmonary arterial pressure in 56 cases of mitral stenosis, is the "PA/chest ratio" studied by Moore *et al.* (13). The "PA/chest ratio" is defined as 100 times the length of a line (x_4 , Fig. 1) originating at and perpendicular to the body midline and terminating at the lateral most aspect of the "pulmonary artery segment," divided by one-half the transthoracic diameter (x_5 , Fig. 1). A regression equation was found which, according to Moore and his associates, provided a fairly accurate estimate of mean pulmonary arterial pressure. The equation correlated less well with the systolic and diastolic pulmonary arterial pressures, pulmonary "capillary" pressure, and pulmonary vascular resistance.

MATERIAL AND RESULTS

Forty-eight patients with pure or predominant mitral stenosis, as established by clinical, laboratory, and cardiac catheterization findings, were investigated. In many the diagnosis was confirmed at surgery. A total of 51 measurements of resting mean pulmonary arterial and pulmonary "capillary" pressure was made, 49 at cardiac catheterization and 2 at thoracotomy. The resting mean pulmonary artery pressure was determined originally by planimetry and more recently by electronic damping.

In each patient a technically satisfactory erect 2-meter postero-anterior chest roentgenogram had been made within a few days of cardiac catheterization (Fig. 1). From this the following data (Table I) were obtained: the presence or absence of B-lines (x_1); the altitude in millimeters of the pulmonary artery segment (x_2); the width in millimeters of the right descending pulmonary artery branch (x_3), by the

TABLE I*

Case No.	Other Valve Lesion	Mean Pulm. Art. Pressure (mm. Hg)	Pulm. Capillary Pressure (mm. Hg.)	x_1 B-Lines (+ = present)	x_2 Height (mm.) Pulm. Art. Segment	x_3 Width (mm.) Desc. Branch Rt. Pulm. Art.	x_4 "PA size" (cm.)	x_5 Internal Thoracic Diam. (cm.)	X
1	...	12	8	0	1	13	3.1	25.5	17.1
2	...	15	12	0	2	13	4.1	24.2	19.1
3	...	16	10	0	—	14	—	26.7	—
4	M.I.	17	12	0	4	15	6.5	27.9	25.5
5	...	17	14	0	3	12	4.0	26.6	19.0
6	...	17	13	0	1	14	5.4	25.3	20.4
7	...	18	—	+ ^a	3	12	4.8	23.5	19.8
8	...	18	13	0	6	15	6.0	29.1	27.0
9	M.I.	20	15	0	—	—	—	29.0	—
10	...	20	11	0	2	14	4.0	27.2	20.0
11	...	20	10	0	4	13	4.5	30.7	21.5
12	...	22	15	0	—	13	—	28.0	—
13	...	23	14	0	5	14	5.1	22.6	24.1
14	...	23	20	0	4	19	5.1	31.7	28.1
15	...	24	22	0	2	12	4.5	26.3	18.5
16	...	25	20	0	3	14	5.1	28.0	22.1
17	M.I.	25	20	0	1	15	4.7	25.4	20.7
18	...	25	15	0	5	13	5.9	28.5	23.9
19	...	28	26	+	2	10	3.7	23.5	15.7
20	M.I.	28	10	0	2	13	—	28.4	—
21	...	28	20	0	2	13	6.1	27.0	21.1
22	...	29	23	0	3	12	5.6	24.3	20.6
23	...	30	18	+	1	13	4.5	25.5	18.5
24	M.I.	30*	29*	+	3	13	5.1	23.3	21.1
25	M.I.	30	19	0	4	12	4.7	25.2	20.7
26	...	31	13	0	4	14	—	24.9	—
27	M.I.	32	23	0	2	14	7.6	30.0	23.6
28	...	34	15	0	3	20	5.3	31.4	28.3
29	...	34	20	0	4	14	4.6	27.9	22.6
30	...	35	28	+	1	12	3.8	22.5	16.8
31	...	37	20	?	4	14	—	26.5	—
32	M.I.	40	27	+	3	13	4.4	26.3	20.4
33	...	44	29	0	8	16	4.8	26.4	28.8
34	...	45	17	0	5	18	7.8	28.1	30.8
35	T.S.	48	28	+	1	16	—	26.1	—
36	M.I.	50	30	+	7	17	4.2	26.0	28.2
37	...	50	21	+	8	21	7.5	29.5	36.5
38	M.I.	50	22	+	6	21	6.2	31.2	33.2
39	...	50	25	+	6	17	5.3	26.0	28.3
40	...	50	33	+	4	22	5.8	27.6	31.8
41	...	50	30	+	6	17	4.1	26.5	27.1
42*	M.I.	55	20	+	5	18	6.6	25.5	29.6
43	...	55	40	+	8	17	5.3	22.5	30.3
44	M.I.	60*	31*	+	8	16	5.8	31.4	29.8
45	...	60	30	+	6	21	6.3	31.0	33.3
46	...	60	30	+	5	19	—	28.7	—
47	M.I.	60	32	+	—	17	—	24.7	—
48	...	62	19	+	7	19	5.8	27.4	31.8
49	...	63	32	+	5	15	6.1	25.0	26.1
50	M.I.	72	—	+	7	19	6.8	30.5	32.8
51	...	85	—	+	5	19	6.8	28.5	30.8

*The abbreviations and symbols in this table require explanation. The abbreviations *M.I.* and *T.S.* signify mitral insufficiency and tricuspid stenosis, respectively. A dash (—) indicates that the corresponding datum was not measured or was not measurable. An asterisk (*) shows that the corresponding pressure value was measured by direct methods at thoracotomy, the value of mean left atrial pressure being listed under the heading of Pulmonary Capillary Pressure. The superscript *a* denotes that B-lines were present before and after cardiac catheterization (Case 7).

technic of Schwedel *et al.*; the "pulmonary arterial size" in centimeters (x_4), by the method of Moore *et al.*; and the internal thoracic diameter (x_5). The value X , representing the sum of the values of x_2 , x_3 , and x_4 , could be determined in 42 of the 51

cases, while in 9 at least one function could not be ascertained. All measurements represent the average of multiple independent mensurations. Cases exhibiting severe scoliosis, emphysema, or pleural effusion were not included.

It was found that the 51 measurements of mean resting pulmonary arterial pressure could be divided into two non-overlapping groups corresponding to (a) pressures below 48 mm. Hg and (b) pressures of 48 mm. Hg and above, depending upon measurements of x_1 , x_2 , and x_3 (Fig. 2). All 16 cases, in which B-lines were present ($x_1 = +$), the height of the pulmonary artery segment (x_2) was 5 mm. or more, and/or the width of the right descending pulmonary artery branch (x_3) was 15 mm.

X = the sum of the numerical values of x_2 , x_3 , and x_4 .

The equations fitted according to the presence or absence of B-lines were:

$$(I) \hat{Y} = 1.04 + 1.794X \text{ when B-lines were present } (x_1 = +)$$

$$(II) \hat{Y} = -15.74 + 1.794X \text{ when B-lines were absent } (x_1 = 0)$$

The estimates of the constant a were found to be significantly different depending upon the presence or absence of B-lines. How-

• = $X_1 +$, $X_2 \geq 5$ mm. and $X_3 \geq 15$ mm. ($n=13$)

◦ = $X_1 +$, $X_2 \geq 5$ mm. or $X_3 \geq 15$ mm. ($n=4$)

○ = cases not meeting above criteria. ($n=34$)

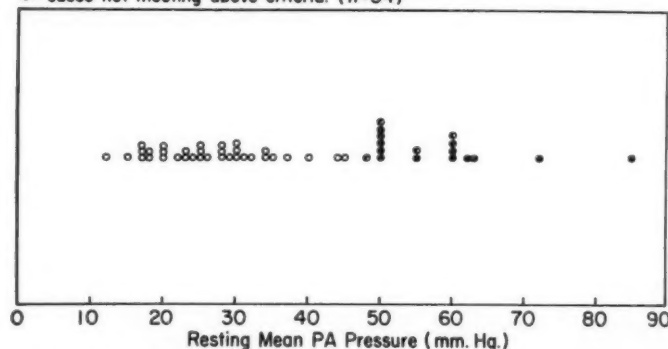


Fig. 2. The 51 mean resting pulmonary arterial pressure measurements could empirically be divided into two groups by employing the roentgenologic criteria shown. The separation point corresponded to a pressure value of 48 mm. Hg.

or greater, were associated with a mean resting pulmonary artery pressure of 48 mm. Hg or higher. No such separation was obtained when x_2 or x_3 was employed as the sole criterion.

The mean resting pulmonary arterial pressure values in 42 persons, of whom 20 exhibited B-lines and 22 did not, were examined as a function of the variables x_2 , x_3 , and x_4 . A variety of functions of these variables was fitted to the data by the method of least squares. The simplest and most useful relationship was found to be of the general form:

$$Y = a + bX$$

where

Y = mean resting pulmonary arterial pressure in mm. Hg and

ever, the estimates of the regression coefficient b did not differ significantly under these two conditions, so that a combined estimate was obtained.

The mean resting pulmonary arterial pressure values and the regression lines are shown in Figures 3 and 4. In each figure the regression line represents the predicted average value of mean pulmonary arterial pressure for any value of X . An increase of one unit in X results in a 1.794 increase in the average value of pressure in both instances. The presence of B-lines is estimated to increase the average value of pressure by 16.78 mm. Hg.

Ninety per cent confidence bands for the true regression lines were calculated and are shown in Figures 3 and 4. The proportion of the total variation in the 42

observed values of pressure accounted for by the presence or absence of B-lines and by the regression of r on X was $r^2 = +0.75$, yielding a multiple correlation coefficient of $r = +0.87$. Also calculated were 90 per cent confidence bands for any single predicted pressure value for a given X ; these are also represented in Figures 3 and 4. The chance that a prediction is in error is 0.10.

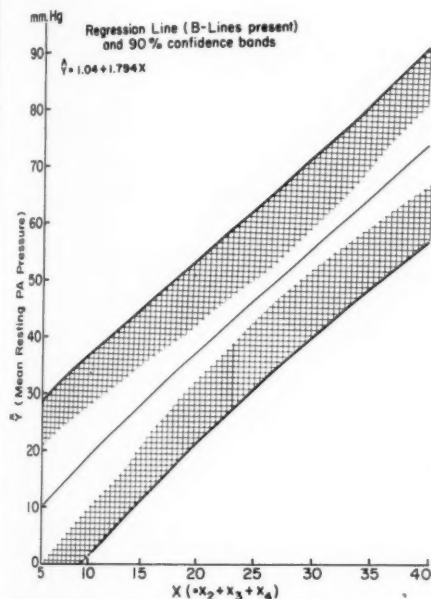


Fig. 3. Regression line for predicting the mean resting pulmonary arterial pressure (\bar{P}) when B-lines are present. The 90 per cent confidence limits for any single predicted value are shown by the heavy outer lines. The 90 per cent confidence bands for the predicted average value for any X lie at the inner margins of the crosshatched areas.

An example of application of these formulas to an average case in point is as follows:

CASE 43: A 22-year-old woman had suffered from known rheumatic heart disease with mitral stenosis for at least five years, with typical cardiac auscultatory and phonocardiographic findings. Roentgenologic examination of the heart disclosed prominence of the pulmonary artery segment ($x_2 = 8$ mm.) and widening of the right descending pulmonary artery branch ($x_3 = 17$ mm.). The "pulmonary artery size" (x_4) was 5.3 cm. Thus X , the sum of these parameters, had a value of 30.3. Since B-lines were present, Formula I was used (Fig. 3). From

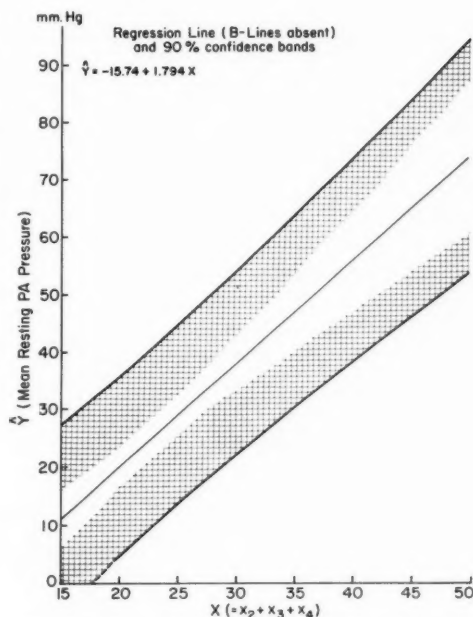


Fig. 4. Regression line for predicting the mean resting pulmonary arterial pressure (\bar{P}) when B-lines are absent. The two pairs of 90 per cent confidence bands are indicated in the same manner as in Fig. 3.

this the value of the mean resting pulmonary arterial pressure with 90 per cent confidence is predicted to lie between 40 and 71 mm. Hg. At cardiac catheterization the observed value was 55 mm. Hg.

When the single roentgen parameters x_2 (height of the pulmonary artery segment) and x_3 (width of the right descending pulmonary artery branch) were individually related to the pulmonary arterial pressure data, a poor correlation was evident, the respective correlation coefficients being $r = +0.67$ and $r = +0.60$. The formula derived by Moore *et al.* (13) was applied to the pulmonary arterial pressure data in the 42 cases in which the "PA/chest ratio" could be established. This gave a correlation coefficient of only $r = +0.42$. Little improvement was obtained when the data in only the 31 cases of pure mitral stenosis were used.

DISCUSSION

If reliable quantitative data are to be derived by roentgenographic measurement, a rigidly controlled reproducible roentgen

technic is required to minimize external variables. Even then such data are to be utilized with caution, since they are affected by non-controllable internal variables, such as depth of inspiration and phase of the cardiac cycle. The patient's clinical status must be stable in the period between chest roentgenography and cardiac catheterization if roentgenologic and hemodynamic measurements are to be correlated.

The use of quantitative roentgenologic criteria minimizes the element of observer interpretation; nevertheless, potential sources of error threaten any observation, and the determination of the presence or absence of B-lines of Kerley is such a danger. Often difficult to demonstrate, these lines may fluctuate in number and intensity, disappearing when pulmonary venous pressure is lowered for whatever reason. Similarly, a sudden temporary rise of pulmonary venous pressure due to acute asymptomatic interstitial pulmonary edema may produce transient B-lines (Grainger, 9). It is also apparent that B-lines cannot reflect venous pressure changes if caused by unrelated processes (see Case 7, Table I).

Conversely, it cannot safely be assumed that hemodynamic measurements are never without error. Technical mishaps such as kinking of the catheter, narrowing or occlusion of its orifice by compression against the arterial wall, and incomplete wedging can produce spurious measurements (Brachfeld *et al.*, 3).

It is recognized that Formulas I and II for prediction of mean resting pulmonary arterial pressure are based upon a relatively small number of observations, which nevertheless compares favorably with other reported series. This may account in part for the considerable separation of the confidence bands and resultant wide range of any predicted pressure values. Inability to reproduce the results of Moore *et al.* (13) with their method suggests that variables in roentgenographic technic or observer interpretation were operative.

Nevertheless, the increasing role of

statistical analysis of medical data appears particularly applicable to areas of investigation such as the diagnosis of heart disease. In the case of mitral stenosis, numerous writers have emphasized the importance of defining the height of pulmonary hypertension as an indication of natural and surgical prognosis (Baker *et al.*, 2; Semler *et al.*, 17). Cardiac catheterization, while a safe and valuable procedure in experienced hands, is to be avoided if a relatively satisfactory method of determination of pulmonary arterial pressure can be substituted, as suggested by Ferrer *et al.* (6). Roentgen examination of the chest is a widely used method of evaluation of rheumatic heart disease and would appear a logical approach for studying further the quantitative values of pulmonary arterial pressure in mitral stenosis.

SUMMARY

1. Roentgenograms of the chest give reliable qualitative evidence of pulmonary hypertension in mitral stenosis, and numerous methods of estimating the degree of hypertension have been devised.

2. By means of chest roentgenograms and pulmonary artery catheterization, correlations were obtained between 51 measurements of mean resting pulmonary arterial pressure and certain quantitative roentgenologic variables in 48 patients.

3. With the use of statistical methods, several objective roentgenologic parameters for the determination of pulmonary arterial pressure were investigated. Regression equations were derived which gave a strong correlation ($r = +0.87$) between mean resting pulmonary arterial pressure and four roentgen parameters: the presence or absence of Kerley's B-lines, the height in millimeters of the pulmonary artery segment, the width in millimeters of the right descending pulmonary artery branch, and the "pulmonary arterial size" in centimeters.

4. Methods described by others for quantitation of pulmonary arterial pressure by roentgenologic measurements were

found to have lower degrees of correlation when applied to the group of patients examined.

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REFERENCES

1. ASSMANN, H.: Über Veränderungen der Hilusschatten im Röntgenbilde bei Herzkrankheiten. *Deutsches Arch. f. klin. Med.* **132**: 355-361, July 13, 1920.
2. BAKER, C., BROCK, R., AND CAMPBELL, M.: Mitral Valvotomy: Follow-up of 45 Patients for Three Years and Over. *Brit. M. J.* **2**: 983-991, Oct. 22, 1955.
3. BRACHFELD, J., REALE, A., AND GOLDBERG, H.: Pitfalls in the Diagnosis of Pulmonary Hypertension. *Am. Heart J.* **55**: 905-918, June 1958.
4. BRUWER, A. J., ELLIS, F. H., JR., AND KIRKLIN, J. W.: Costophrenic Septal Lines in Pulmonary Venous Hypertension. *Circulation* **12**: 807-812, November 1955.
5. CARMICHAEL, J. H. E., JULIAN, D. G., PENRHYN JONES, G., AND WREN, E. M.: Radiological Signs in Pulmonary Hypertension: Significance of Lines B of Kerley. *Brit. J. Radiol.* **27**: 393-397, July 1954.
6. FERRER, M. I., AND OTHERS: Circulatory Effects of Mitral Commissurotomy with Particular Reference to Selection of Patients for Surgery. *Circulation* **12**: 7-29, July 1955.
7. FLEISCHNER, F. G., AND REINER, L.: Linear X-Ray Shadows in Acquired Pulmonary Hemosiderosis and Congestion. *New England J. Med.* **250**: 900-905, May 27, 1954.
8. FLEMING, P. R., AND SIMON, M.: The Haemodynamic Significance of Intrapulmonary Septal Lymphatic Lines (Lines B of Kerley). *J. Fac. Radiologists* **9**: 33-36, January 1958.
9. GRAINGER, R. G.: Pulmonary Hypertension: A Symposium. III. Interstitial Pulmonary Oedema and its Radiological Diagnosis. A Sign of Pulmonary Venous and Capillary Hypertension. *Brit. J. Radiol.* **31**: 201-217, April 1958.
10. GRISHMAN, A., JICK, S., AND KHLNANI, M. T.: The Pulmonary Radiographic Changes of Mitral Disease: Mitral Lung Disease. *J. Mt. Sinai Hosp.* **25**: 291-304, July-August 1958.
11. KERLEY, P.: Radiology in Heart Disease. *Brit. M. J.* **2**: 594-597, Sept. 30, 1933.
12. LEVIN, B.: On the Recognition and Significance of Pleural Lymphatic Dilatation. *Am. Heart J.* **49**: 521-537, April 1955.
13. MOORE, C. B., KRAUS, W. L., DOCK, D. S., WOODWARD, E., JR., AND DEXTER, L.: The Relationship Between Pulmonary Arterial Pressure and Roentgenographic Appearance in Mitral Stenosis. *Am. Heart J.* **58**: 576-581, October 1959.
14. ROSSALL, R. E., AND GUNNING, A. J.: Basal Horizontal Lines on Chest Radiographs: Significance in Heart Disease. *Lancet* **1**: 604-606, May 5, 1956.
15. ROUSSEL, J., PERNOT, C., SCHOUMACHER, P., AND PERNOT, M.: Les signes radiologiques de l'hypertension artérielle pulmonaire. *J. de radiol.* **40**: 469-477, August-September 1959.
16. SCHWEDEL, J. B., ESCHER, D. W., AARON, R. S., AND YOUNG, D.: The Roentgenologic Diagnosis of Pulmonary Hypertension in Mitral Stenosis. *Am. Heart J.* **53**: 163-170, February 1957.
17. SEMLER, H. J., SHEPHERD, J. T., AND WOOD, E. H.: The Role of Vessel Tone in Maintaining Pulmonary Vascular Resistance in Patients with Mitral Stenosis. *Circulation* **19**: 386-394, March 1959.
18. SHORT, D. S.: Radiology of the Lung in Left Heart Failure. *Brit. Heart J.* **18**: 233-240, April 1956.
19. WHITAKER, W., AND LODGE, T.: The Radiological Manifestations of Pulmonary Hypertension in Patients with Mitral Stenosis. *J. Fac. Radiologists* **5**: 182-188, January 1954.

SUMMARY IN INTERLINGUA

Roentgeno-Evaluation del Tension Pulmono-Arterial in Stenose Mitral

Roentgenogrammas del thorace provide solide informationes qualitative in re le hypertension pulmonar in stenose mitral, e numerose methodos ha essite elaborate pro estimar etiam le grado de ille hypertension.

Per medio de roentgenogrammas thoracic e catheterisationes de arteria pulmonar, correlationes esseva obtenite inter 51 mesurationes del tension pulmono-arterial medie in stato de reposo e certe quantitative variabiles roentgenologic in 48 patientes.

Per medio de methodos statistic, plure objective parametros pro le determination del tension pulmono-arterial esseva investigate. Equationes de regression esseva derivate que monstrava un forte cor-

relation ($r = +0.87$) inter le tension pulmono-arterial medie in stato de reposo e quattro parametros roentgenographic: le presentia o absentia de lineas B de Kerley, le altor in millimetros del segmento pulmono-arterial, le largor in millimetros del branca dextero-descendente del arteria pulmonar, e le "dimension del arteria pulmonar" in centimetros.

Esseva trovate que le methodos describe pro altere autores pro le quantitation del tension pulmono-arterial super le base de mesurationes roentgenologic resultava in plus basse grados de correlation in lor application al gruppo de patientes hic examine.

An Evaluation of Cardiovascular Contrast Media¹

J. STAUFFER LEHMAN, M.D., and JOSEPH N. DEBBAS, M.D.

THE INCREASING application of cardiovascular opacifying procedures to the diagnosis of congenital malformations of the heart and great vessels and to the study of acquired cardiovascular disease has promoted an acceleration of effort toward the search for and formulation of more satisfactory radiopaque media. Within recent years, a number of compounds and formulations of newer types have been introduced while, at the same time, there has been progress in the development of additional opacifying procedures and techniques for the diagnosis of congenital heart disease and disease states of the cardiac valves, coronary arteries, and pulmonary circulation. None of our present-day methods of cardiovascular opacification is completely devoid of danger to the patient; none is wholly innocuous. In large measure, the inherent hazards relate to the injected radiopaque medium. In the amounts and dosages necessary for effective opacification, any or all of the currently employed radiopacifying agents can, on occasion, produce undesirable reactions and complications.

It has therefore seemed pertinent to give further consideration to certain of the physicochemical and toxicological properties of the various cardiovascular contrast materials we have employed in our clinical studies of the heart, intrathoracic vessels, and pulmonary circulation. While we have used all of the media listed in Table I in certain studies of the abdominal aorta and its branches, we have, for purposes of this publication, restricted our comments to those related to opacification of the heart and intrathoracic vessels. When the site of delivery of the opaque medium is the lower thoracic or upper abdominal aorta,

considerations arise as to toxic effects upon the kidneys and intestines. Injections made some distance proximal to the origins of the renal and intestinal arterial supply permit a degree of radiopaque dilution, and hence these problems are of less concern. The majority of reactions and deleterious physiological effects produced by intracardiac or intrathoracic vascular opacifications are due to the transport to and effects of the injected media upon the central nervous system. Full deliberation must therefore be given to the neurotoxic properties of the radiopaque substances.

There is a considerable literature dealing with the effect of various radiopaque agents upon the central nervous system. Included among the publications are articles relating to cerebral angiography in relation to the blood-brain barrier (1, 5, 6, 37), techniques for pharmacodynamic investigation of contrast media (7, 31), the physiological effects of various media (2, 3, 14, 16-21, 25, 28, 35), cardiovascular responses (11, 27), and clinical evaluation studies (4, 12, 13, 23, 29, 36, 39, 40). Important data are contained in these publications. Fischer and Eckstein (11) have recently summarized the major contributions comparing cerebral angiographic contrast media and have made their own experimental comparison of certain of these agents. They studied the alterations in arterial pressure, venous pressure, heart rate and rhythm, electrocardiographic recording, and the end-expiratory CO₂ concentration incident to controlled intracarotid injections of a number of radiopaque media of equal iodine content in dogs.

In addition to extensive studies of the

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TABLE I: CARDIOVASCULAR RADIOPAQUE MEDIA

Medium	Wt./ Vol. (per cent)	Generic Name	Chemical Name	Mg. Chemical/c.c. of Solution (Wt./Vol.)	Iodine Content of Solution (per cent)
Urokon Sodium 50% (Mallinckrodt)	50	Sodium acetrizoate	Sodium salt of 3-acetamido-2,4,6-triiodobenzoic acid	500	32.9
Urokon Sodium 70% (Mallinckrodt)	70	Sodium acetrizoate	Sodium salt of 3-acetamido-2,4,6-triiodobenzoic acid	700	46.0
Miokon Sodium 50% (Mallinckrodt)	50	Sodium diprotrizoate	Sodium salt of 3,5-dipropionyl-amino-2,4,6-triiodobenzoic acid	500	28.6
Ditriokon (Mallinckrodt)	68.1	Sodium diprotrizoate, 31.4% Sodium diatrizoate, 36.7% Sodium diatrizoate, 8.0% Methylglucamine diatrizoate, 52.0%	Sodium salt of 3,5-dipropionyl-amino-2,4,6-triiodobenzoic acid Sodium salt of 3,5-diazetyl-amino-2,4,6-triiodobenzoic acid Sodium and methylglucamine salts of 3,5-diacetyl-amino-2,4,6-triiodobenzoic acid	680	40.0
Renografin 60% (Squibb)	60	Sodium diatrizoate, 8.0% Methylglucamine diatrizoate, 52.0%	Sodium and methylglucamine salts of 3,5-diacetyl-amino-2,4,6-triiodobenzoic acid	600	29.26
Renografin 76% (Squibb)	76	Sodium diatrizoate, 10.0% Methylglucamine diatrizoate, 66.0%	Sodium and methylglucamine salts of 3,5-diacetyl-amino-2,4,6-triiodobenzoic acid	760	37.0
Cardiografin 85% (Squibb)	85	Methylglucamine diatrizoate	Methylglucamine salt of 3,5-diacetyl-amino-2,4,6-triiodobenzoic acid	850	40.0
Renovist* (Squibb)	69.3	Sodium diatrizoate, 35% Methylglucamine diatrizoate, 34.3%	Sodium and methylglucamine salts of 3,5-diacetyl-amino-2,4,6-triiodobenzoic acid	693	37.2
Diodrast 70% (Winthrop)	70	Iodopyracet	Diethanolamine salt of 3,5-diiodo-4-pyridone-N-acetic acid	700	34.8
Hypaque Sodium 50% (Winthrop)	50	Sodium diatrizoate	Sodium 3,5-diacetamido-2,4,6-triiodobenzoate	500	30.0
Hypaque-M 75% (Winthrop)	75	Sodium diatrizoate, 25% Methylglucamine diatrizoate, 50%	Sodium and methylglucamine salts of 3,5-diacetamido-2,4,6-triiodobenzoic acid	750	38.5
Hypaque-M 90% (Winthrop)	90	Sodium diatrizoate, 30% Methylglucamine diatrizoate, 60%	Sodium and methylglucamine salts of 3,5-diacetamido-2,4,6-triiodobenzoic acid	900	46.2

* Not yet commercially available.

various contrast substances used in cerebral angiography, a review of the literature shows numerous investigations of media developed within the past decade for utilization in intravenous urography (10, 32-34, 38) and, to a lesser extent, in angiocardiology (8, 9, 24), coronary arteriography (15), aortography, and peripheral angiography (26, 30).

METHOD OF INVESTIGATION

As previously mentioned, the present study relates to radiopaque media employed for intrathoracic cardiovascular opacification procedures.

Since an ideal cardiovascular radiopaque agent should possess good radiodensity, low viscosity and hence easy injectability,

and an absence or low degree of toxicity, we have studied the media we have employed from the standpoint of viscosity, flow rates through catheters, certain animal tolerance determinations, phantom radiodensity, and comparative angiographic opacification in experimental animals (dogs). Finally, we have tabulated the reactions observed in a group of clinical studies with certain of the media. Table I lists the radiopaque media we have used for intrathoracic cardiovascular opacification procedures. The Table shows the percentage concentrations (weight/volume); the name of the manufacturer; the generic name and, in the case of mixtures of two chemical compounds, the percentages of each (weight/volume); the

chemical name; the milligrams of chemical per cubic centimeter of solution (weight/volume), and the iodine content in percentage of the solution. All of these media are available commercially, except Renovist,² which has at the time of this report not yet been released for commercial distribution.

It will be noted that, with the exception of Urokon Sodium 50 per cent, Urokon Sodium 70 per cent, Miokon, and Diodrast 70 per cent, all contain a diatrizoate compound. The Urokon, Miokon, and Diodrast have been available for some years. Those media containing diatrizoate compounds are of more recent formulation. Renografin 60 per cent, Renografin 76 per cent, Renovist, Hypaque 75 per cent, and Hypaque 90 per cent³ represent various admixtures of the sodium and methylglucamine salts of diatrizoic acid. Cardiografin 85 per cent² contains as its salt only methylglucamine, while Hypaque 50 per cent³ is the sodium salt. Ditrion⁴ is a mixture of the constituent of Miokon (sodium diprotrizoate) and the sodium salt of diatrizoic acid.

Each formulation represents an effort to achieve the most satisfactory combination of radiopacity, injectability, and radiodensity, with absence of adverse patient reaction.

Viscosity: In our own laboratories, we have made viscosity determinations on the radiopaque solutions listed in Table II. The determinations were conducted at temperatures of approximately 25°, 38°, and 45° C. A Brookfield viscometer⁵ was used. The viscosities of the tested solutions, in centipoises, at the various temperatures are shown in Table II. It is to be noted that in our determinations, Hypaque Sodium 50 per cent has the lowest and Cardiografin 90 per cent the highest viscosity.

² Generously supplied by E. R. Squibb & Sons, New Brunswick, N. J.

³ Generously supplied by Winthrop Laboratories, New York, N. Y.

⁴ Generously supplied by Mallinckrodt Chemical Works, St. Louis, Mo.

⁵ Manufacturer, Brookfield Engineering Laboratories, Stoughton, Mass.

TABLE II: VISCOSITY OF RADIOPAQUE MEDIA IN CENTIPOISES

Radiopaque Medium	25° C.	38° C.	45° C.
	(24.4-25.6°)	(38.0-39.8°)	(44.2-45.8°)
Hypaque Sodium 50%	3.25	2.34	2.02
Miokon Sodium 50%	3.81	2.70	2.21
Diodrast 70%	5.34	3.86	2.88
Renografin 60%	5.60	3.92	3.20
Urokon Sodium 70%	6.56	4.31	3.44
Ditrion	8.15	5.33	4.09
Renovist	9.10	6.12	4.73
Hypaque-M 70%	10.48	6.62	5.08
Hypaque-M 75%	13.40	8.35	6.62
Renografin 76%	13.94	9.10	6.98
Hypaque-M 80%	19.37	11.16	8.14
Cardiografin 85%	23.40	13.72	9.24
Hypaque-M 85%	25.30	14.28	10.30
Hypaque-M 90%	33.75	18.70	12.50
Cardiografin 90%	42.75	22.95	16.00

The influence of temperature on viscosity is quite apparent, the more viscous media showing a larger proportional decrease in viscosity as temperature is raised from 25 to 45° C. In clinical practice, it is our regular custom to preheat all cardiovascular opaque media to at least 38° C. Very frequently we have injected the solution at 45° C., and occasionally at 60° C., and have observed no sequelae related to these higher temperatures.

In experimental animal studies, injections at 60° C. have produced no demonstrable untoward effects. It is our belief that a two-second injection of 50 c.c. of currently employed media into a cardiac chamber or into the aorta of living man, at a temperature as high as 60° C., does not cause any local tissue damage, physiological aberration, or generalized systemic reaction related to the temperature of the injected material. It is reasonable to assume that there is such rapid heat dispersion in the moving opaque column that local tissue damage is quite improbable.

Flow Rates Through Catheters: We are concerned, in clinical practice, with the problem of rapid injection of a radiopaque medium. In many intrathoracic cardiovascular opacification procedures, injection is by way of a catheter of small lumen. The flow rates of fluids through small-bore tubing are basically governed by Poiseuille's law, commonly expressed as

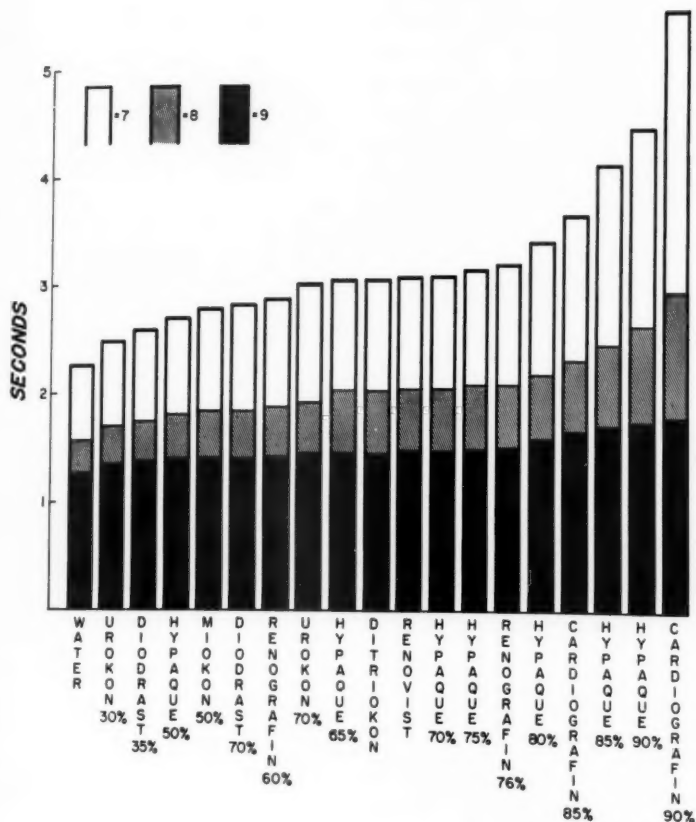


Fig. 1. Catheter flow rates for various radiopaque media.

$$Q = \frac{\pi PR^4}{8\eta L}$$

where

Q = Quantity flow per unit of time as expressed in cubic milliliters per second

P = Applied pressure in dynes per cubic centimeter

R = Radius of the tube in centimeters

η = Coefficient of viscosity in poises

L = Length of the tube in centimeters

Clinically, this formula must be applied with some care, since it involves two basic assumptions: (a) that there is laminar flow or, in other words, a fluid motion that is sufficiently slow to avoid turbulence, which may be reached at certain velocities and is also dependent upon the diameter of the tube, the fluid density, and its viscosity; (b) that the tube is of sufficient rigidity that there is no distention to cause any change in its radius, since in

Poiseuille's law, a small increase in R causes a large increase in Q . These conditions do not hold strictly for many catheter cardiovascular opacification studies.

While a variety of catheters are employed in clinical cardiovascular opacification procedures, it is common practice to use a nylon, woven, thin-wall type. The Lehman aortography catheter,⁶ introduced in 1949, is of this type. However, it was originally designed with a single end opening. The later NIH and Rodriguez-Alvarez modifications⁶ have closed ends with multiple side holes located in their distal portion.

We have determined flow rates of a number of types and concentrations of radiopaque media through NIH catheters.

⁶ Manufactured by United States Catheter and Instrument Company, Glens Falls, N. Y.

Figure 1 is a composite block graph showing the tested agents and their flow rates through F7, F8, and F9 NIH catheters of 100 cm. length. A Gidlund pneumatic pressure injector⁷ at its maximal injection pressure of 10 kg./cm.² was used in each testing. The amount of medium for each testing was 50 c.c., and the temperature of each solution was 38° C.

It is of interest that with a large-bore catheter (F9), at the high injection pressure applied, the rate of flow of each of the tested solutions closely approximates that of water. As the catheter bore is decreased, differences in rate of flow become more evident. Of the substances we have tested, Cardiografin 90 per cent has the slowest rate of flow, while two solutions which we have used only occasionally (Hypaque-M 50 per cent and Miokon Sodium 50 per cent) have the most rapid rates, as measured by our catheter flow rate studies.

As would be expected, flow rates through catheters are influenced by the temperature of the medium. Certain curves illustrating these temperature influences have been published by one of us (22).

Animal Toxicity Studies: In the amounts and dosages commonly administered in clinical cardiovascular opacification procedures, all of the currently available contrast media can produce systemic reactions; none is completely innocuous. Somewhat dependent upon the chemical nature and concentration of the contrast agent, to a larger degree upon the amount injected, and, to a certain extent upon the site of the injection, cerebrototoxic and cardiotoxic effects may result. Since, in general, the larger the injected dose the more adequate the resultant opacification, and since there are occasions with certain procedures when it is advantageous to make multiple injections, a knowledge of the amounts of the various opaque media which may produce irreversible damage or even fatality is of vital importance.

In the formulation and testing of any

contrast agent, all pharmaceutical manufacturers determine toxicity by animal experiments. The results of these determinations are readily available through the manufacturer.

We have been interested in making toxicity comparisons of two newer preparations (Ditriakon and Renovist), which we have recently been using in clinical opacification studies, with two of the older media (Diodrast 70 per cent and Urokon 70 per cent) which we previously utilized. Our studies have not been sufficiently extensive to determine the LD 50 of each tested medium in our experimental set-up. We have, however, investigated the amount of Renovist and of Ditriakon which could be administered intravenously to dogs in a period of one minute without lethal effect, and the amounts which would be fatal in the majority of the tested animals.

Selecting the highest nonlethal dose for both Renovist and Ditriakon, we tested this dose level with Diodrast 70 per cent and Urokon 70 per cent. The details of the experiment are as follows: Healthy adult mongrel dogs, ranging in weight from 7.2 to 15.8 kg., were selected at random. Each dog was anesthetized with 30 mg. of phenobarbital per kilogram of body weight. A large-bore polyethylene tube or an F9 catheter was inserted into the right femoral vein. In the initial stages of our study, we also cannulated the right femoral artery for systemic blood pressure determinations, but we later abandoned this after having obtained an appreciation of the usual pressure changes incident to intravenous high-dosage radiopaque injections.

Electrocardiographic monitoring and recording were maintained, utilizing Lead 2, both prior to, throughout, and for one minute after the radiopaque injection; as well as at two-, three-, and five-minute post-injection intervals. This monitoring was continued if there was a persistent aberration of the electrocardiographic pattern. Respiratory rates were observed and recorded at these same intervals.

All of the tested radiopaque media were

⁷ Distributed by Schick X-ray Corporation, Chicago, Ill.

TABLE III: TOXICITY STUDIES OF RADIOPAQUE MEDIA

Radiopaque Medium	Dose c.c./ kg.	Dose mg./ kg.	No. of Dogs	Fatal- ities	Remarks
Diodrast 70%	10	7,000	8	8	Death occurred at 2, 3, 7, 8, 10, 16, and 18 min., and 6 hr. post-injection. Respiratory arrest predominant. Convulsions, 6 hr. duration (1 dog).
Urokon 70%	10	7,000	8	6	The 2 animals recovering had convulsions for 6 and 30 hr., respectively. Six deaths occurred at 2, 3, 3, 3, 4 min. and 6.5 hr. post-injection. Respiratory arrest predominant. Convulsions, 6.5 hr. duration (1 dog).
Urokon 70%	13	9,100	8	8	Deaths occurred at 2, 4, 6, 7, 8, and 20 min. and 6 and 12 hr. post-injection. Respiratory arrest predominant. Convulsions, 6 and 12 hr. duration (2 dogs).
Ditriokon	10	6,800	8	0	Seven uneventful recoveries. Convulsions, 1 hr. duration (1 dog), with complete recovery.
Ditriokon	13	8,840	8	2	Six uneventful recoveries. Two deaths occurred at 4 and 30 min. post-injection.
Ditriokon	15	10,200	8	4	Four uneventful recoveries. Four deaths occurred at 2, 3, and 4 min. and 3.5 hr. post-injection.
Renovist	10	6,930	8	0	Eight uneventful recoveries.
Renovist	13	9,009	8	1	Six uneventful recoveries. One ataxia for 16 hr., with complete recovery. One death occurred 5 min. post-injection.
Renovist	15	10,395	8	6	Two uneventful recoveries. Six deaths occurred at 2, 3, 4, 6, 8, and 17 min. post-injection.

preheated to body temperature, and the entire predetermined dosage was, in each instance, injected in exactly one minute. Observations were made as to reactions, such as alterations in respiration, heart rate, electrocardiographic changes, and evidence of neurotoxic effects. If the animal survived, it was watched for three hours, and at regular intervals over a forty-eight hour period, or until it had completely recovered and returned to apparently normal status. Initially, Renovist and Ditriokon were both given at graduated dose levels of 2, 4, 6, 8, and 10 c.c. per kilogram of body weight. Having determined that we could regularly expect survival of the animal when a dose of 10 c.c. per kilogram of either medium was administered, we studied this same dosage level of Diodrast 70 per cent and Urokon 70 per cent. We then gave doses of 13 c.c. per kilogram of body weight, using Urokon 70 per cent, Renovist, and Ditriokon, and 15 c.c. per kilogram of body weight with Renovist and Ditriokon. For each dose level series and for each of the five radiopaque solutions tested, a separate dog was utilized for each injection. Table III summarizes the observations.

In this table, the dose for each of the series of testings is given as both cubic

centimeters and milligrams of the chemical per kilogram of body weight. While the practicing radiologist is interested in the volume or size of the bolus delivered, he should have knowledge of the amount of chemical compound injected. This is particularly pertinent in considerations of reactions and toxic effects. A uniform practice of reporting both the volume (cubic centimeters) of administered solution and the weight (milligrams) of chemical constituent in terms of units (kilograms) of body weight would add clarity to the literature dealing with administration of radiopaque media.

It is noteworthy that Diodrast 70 per cent administered at a dose level of 10 c.c./kg. (7,000 mg./kg.) proved fatal to all dogs. Urokon 70 per cent at the 10 c.c./kg. (7,000 mg./kg.) level led to death in 6 of 8 dogs, and the 2 survivors exhibited marked neurotoxic effects with, however, final apparently complete recovery.

Ditriokon in the 10 c.c./kg. (6,800 mg./kg.) dose brought about no fatalities, but there was one instance of post-injection convulsion.

There were no fatalities among the dogs given Renovist at the 10 c.c./kg. (6,930 mg./kg.) level, and there were no convulsive manifestations.

With Urokon at 13 c.c./kg. (9,100 mg./kg.) all dogs died. Of 8 dogs given Ditriokon at 13 c.c./kg. (8,840 mg./kg.) 2 died. There was one death among 8 of the animals receiving 13 c.c./kg. (9,009 mg./kg.) of Renovist.

With Ditriokon at 15 c.c./kg. (10,200 mg./kg.) 4 (or one-half) of the dogs expired; while at a 15 c.c./kg. (10,395 mg./kg.) dosage of Renovist, 6 of 8 dogs died.

The number of dogs tested in each group is obviously too small to permit of statistically valid comparison where there were some survivals and some fatalities. However, we do consider that the situations in which all dogs survived or all expired are

TABLE IV: DENSITOMETRIC STUDIES

Radiopaque Medium	Densitometer Reading
Lower Range Radiopacity	
Renografin 60%	0.750
Miokon Sodium 50%	0.710
Hypaque Sodium 50%	0.700
Medium Range Radiopacity	
Renovist	0.595
Hypaque-M 70%	0.585
Renografin 76%	0.575
Ditriokon	0.570
Hypaque-M 75%	0.550
Cardiografin 85%	0.525
Hypaque-M 80%	0.500
Higher Range Radiopacity	
Diodrast 70%	0.450
Hypaque-M 85%	0.420
Hypaque-M 90%	0.410
Cardiografin 90%	0.400
Urokon Sodium 70%	0.300

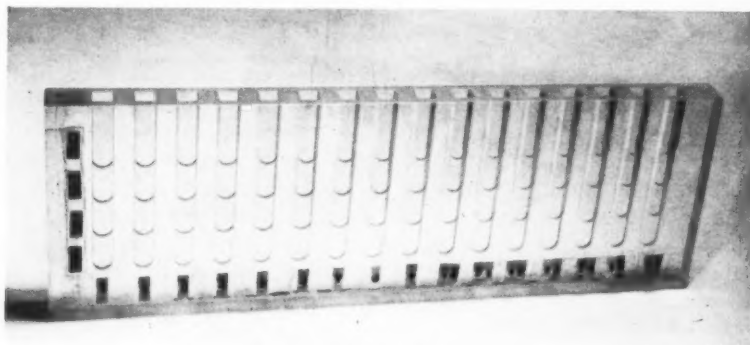


Fig. 2. Plastic block phantom.

significant. It is thus evident that Urokon 70 per cent and Diodrast 70 per cent are more toxic than either Renovist or Ditriokon.

Radiodensity: The radiodensity of all media currently employed for intravascular-intracardiac opacification procedures depends upon their iodine content. The percentage iodine content of the currently used solutions is, as mentioned above, listed in Table I. We have given attention to the degree to which the differences in iodine content of the respective solutions can be reflected, by experimental studies utilizing certain radiographic technics. For this purpose, we have devised a cell phantom which is illustrated in Figure 2. The phantom consists of a plastic block with 16 cell compartments, each of which

has been meticulously machined in graduated steps of cell thickness of 1/8 inch, 1/4 inch, 3/8 inch, and 1/2 inch.

Cell No. 1 was filled with water; each of the other 15 cells was filled with a different radiopaque solution, thus providing a phantom in which four thicknesses of each of the various solutions could be studied simultaneously as to radiodensity. Using Eastman Blue Brand X-ray Film and a cassette with Patterson par speed intensifying screens, we radiographed the entire block of 16 cells and their contained solutions. The radiographic studies were conducted at 40-, 60-, 80- and 100-kv levels, with appropriate adjustment of the mas values to effect comparable studies at each kilovolt level. The distance factor was standardized at 72 inches. The

radiographic density studies were performed both without filter and with 2 mm. of aluminum filtration, and also with a phantom of 10 cm. of Presdwood (Fig. 3) interposed between the x-ray tube and the radiopaque-containing phantom. The mas factors were appropriately adjusted for comparable radiographic densities. Figure 4 is a typical radiograph resulting from such studies.

The radiographic densities of the various opaque media were recorded by means of an electronic densitometer.⁸ Utilizing the several film densitometric studies made at the various kilovolt levels, with and without the aluminum filtration and Presdwood phantom, we constructed a composite

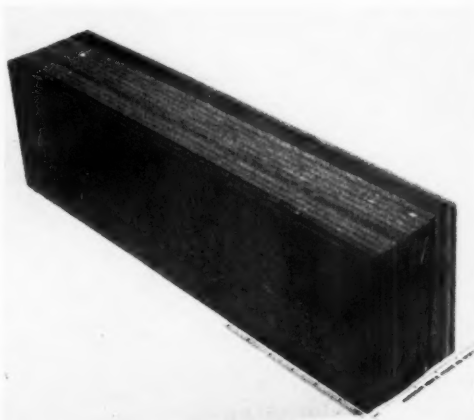


Fig. 3. Presdwood phantom.

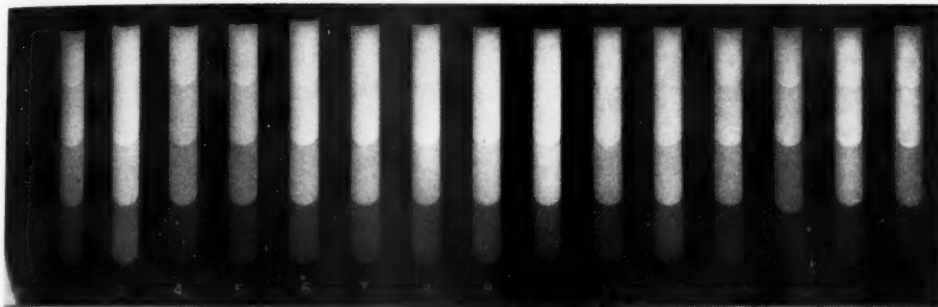


Fig. 4. Radiograph of plastic block phantom. Cells contain: (1) water; (2) Diodrast 70 per cent; (3) Urokon 70 per cent; (4) Miokon 50 per cent; (5) Hypaque 50 per cent; (6) Hypaque 70 per cent; (7) Hypaque 75 per cent; (8) Hypaque 80 per cent; (9) Hypaque 85 per cent; (10) Hypaque 90 per cent; (11) Cardiografin 85 per cent; (12) Cardiografin 90 per cent; (13) Renovist; (14) Renografin 60 per cent; (15) Renografin 76 per cent; (16) Ditiokion.

table of the densitometric measurements of the tested radiopaque solutions (Table IV). It is an accepted observation that the electronic method of determining varying degrees of radiographic blackening of an x-ray film is more sensitive than visual determinations.

All of the tested solutions in their various concentrations were procured, in sealed vials, from the several manufacturers. Minor differences in their radiodensity might, on occasion, be attributable to problems inherent in the manufacture and packaging of exact concentrations of radiopaque solution. In our experimental studies, we utilized the films, cassettes,

and screens which we normally employ for clinical procedures in an effort to approximate as closely as possible the conditions which maintain in clinical practice.

The figures shown in Table IV are arbitrary values. The higher figures represent the least degree of radiodensity; the lowest represents the greatest radiodensity. Thus, Renografin 60 per cent, Miokon Sodium 50 per cent and Hypaque Sodium 50 per cent occupy the lower range of radiodensity as adjudged by these determinations, while Urokon Sodium 70 per cent is of the greatest radiodensity. It is worthy of note that on visual inspection of the cell-block studies we can differentiate the radiodensities of a number of the

⁸ Densichron, manufactured by the W. M. Welch Scientific Company, Chicago, Ill.

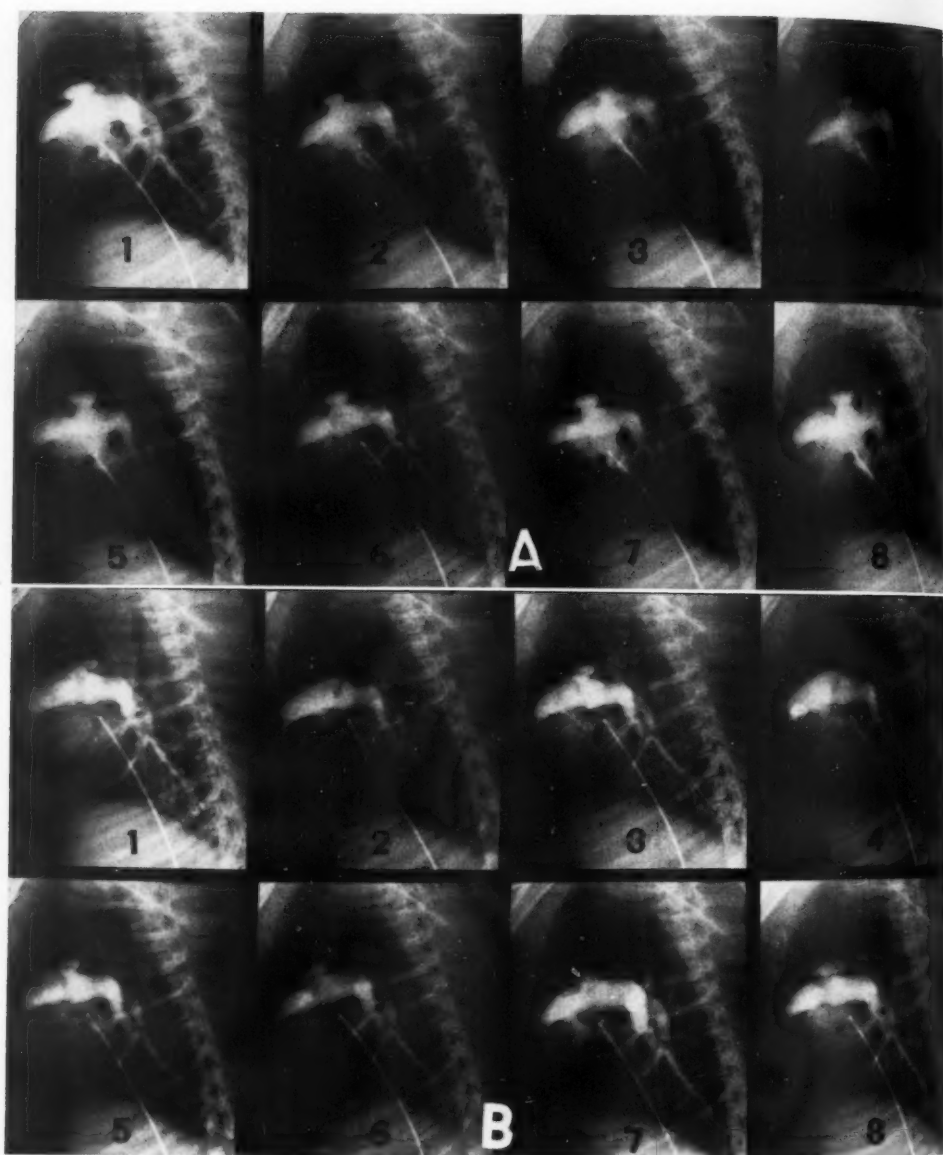


Fig. 5. A and B. Angiocardiograms of a dog, obtained with eight different radiopaque solutions: (1) Hypaque 90 per cent; (2) Hypaque 50 per cent; (3) Ditiokon; (4) Renovist; (5) Renografin 76 per cent; (6) Renografin 60 per cent; (7) Urokon 70 per cent; (8) Cardiografin 85 per cent.

A. Early dextro phase at 1.2 seconds.

B. Dextro and pulmonary arterial filling phase at 2.0 seconds.

radiopaque solutions. Thus, there is a definite and easily discernible difference between Hypaque 50 per cent and Hypaque 90 per cent. On close scrutiny, the difference between Hypaque 75 per cent and

Hypaque 90 per cent is also evident. It is difficult to distinguish visually any differential density between Renovist, Hypaque 70 per cent, Renografin 76 per cent, Ditiokon, Hypaque 75 per cent,

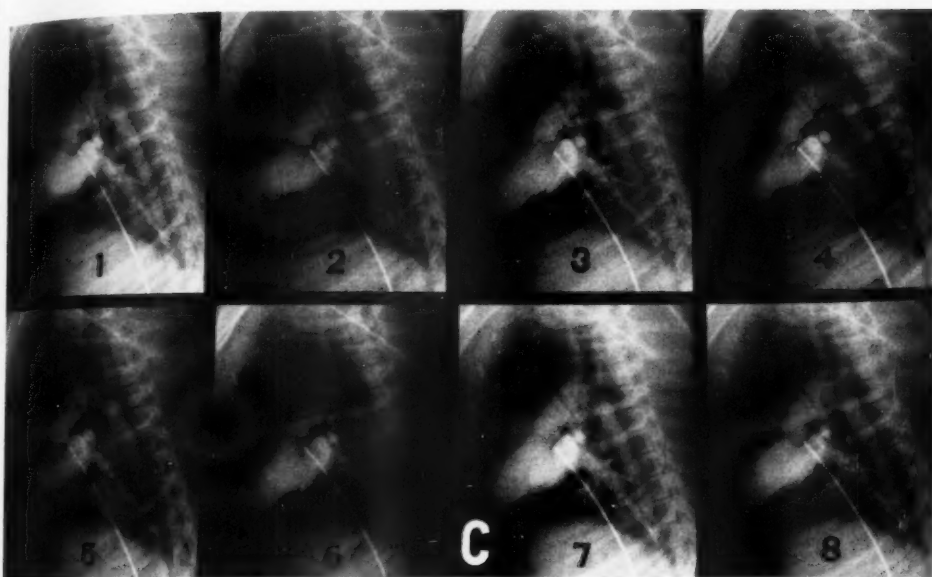


Fig. 5, C. Angiocardiacogram of a dog obtained with eight different radiopaque solutions (see Fig. 5, A and B). Levo phase at 4.0 seconds.

Cardiografin 85 per cent, and Hypaque 80 per cent.

While the cell-block type of study offers some basis for evaluation of the ability to distinguish visually between the radiodensities of several radiopaque solutions, in clinical radiology we are concerned with the effective opacification of the anatomical part under investigation and, in the case of intrathoracic cardiovascular opacification studies, with the relative opacifying properties of various media as regards the cardiac chambers, coronary arteries, intrathoracic vessels, and the cardiac and vascular structures.

In order to determine whether there are major distinguishable differences in the radiopacity of one solution as compared with another or others, under conditions simulating those of clinical cardiovascular opacification studies, we set up the following testing procedure: Healthy dogs weighing 11 to 15 kg. were anesthetized with phenobarbital. An F7 NIH type catheter, 100 cm. in length, was introduced via the right femoral vein and its tip positioned in the right atrium. With a Gidlund pneumatic pressure injector, radio-

paque solution in a dose of 1.0 c.c. per kilogram of body weight was injected in two seconds. Rapid serial filming (4 films per second) in lateral projection was performed over a seven-second period. This filming covered the injection interval and continued through the dextro- and levo-phases of the angiocardiacographic study. Eight different radiopaque agents were employed for each dog (Hypaque 90 per cent, Hypaque 50 per cent, Ditiokon, Renovist, Renografin 76 per cent, Renografin 60 per cent, Urokon 70 per cent and Cardiografin 85 per cent). The solutions were selected at random for each animal. Electrocardiographic monitoring was maintained to assure that there was relatively uniform heart rate throughout each 8-injection procedure. Four dogs were studied in this manner. The radiographic factors were: kv, 65 to 75; ma, 500; exposure, 1/120th second; distance, 30 inches. A Franklin serialograph⁹ was used, with filming rate of 4 per second for seven seconds. Each filming series was then carefully compared with each of the 7 other

⁹ Manufactured by Franklin X-ray Company, Philadelphia, Penna.

TABLE V-A: CLINICAL STUDIES WITH HYPAGUE.

Procedure	Radiopaque Medium	Number of Patients	Age Range
Selective Catheter Angiocardiology	Hypaque-M 75% Renovist Ditriakon	14 (6)* 30 (17)* 12 (5)*	10 da.-62 yr. 10 wk.-82 yr. 4 mo.-67 yr.
Venous Abdominal Aortography	Renovist	5	15 yr.-60 yr.
Catheter Thoracic Aortography	Renovist Ditriakon	34 (4)* 5	5 yr.-67 yr. 22 yr.-67 yr.
Coronary Arteriography	Renovist Ditriakon	26 5	32 yr.-67 yr. 25 yr.-44 yr.
Cardiac (Catheter) Ventriculography—Left	Renovist Ditriakon	15 3	16 yr.-52 yr. 35 yr.-51 yr.
Cardiac (Needle) Ventriculography—Left	Renovist Ditriakon	4 3	21 yr.-50 yr. 32 yr.-48 yr.
Cardiac (Catheter) Ventriculography—Left/Catheter Thoracic Aortography	Renovist Ditriakon	34 3	20 yr.-60 yr. 13 yr.-40 yr.
Selective Catheter Angiocardiology/Catheter Thoracic Aortography	Renovist	5 (1)*	12 yr.-58 yr.
Selective Catheter Angiocardiology/Cardiac (Catheter) Ventriculography—Left	Renovist	7	16 yr.-45 yr.
Selective Catheter Angiocardiology/Cardiac (Catheter) Ventriculography—Left/Catheter Thoracic Aortography	Renovist	3	14 yr.-22 yr.
TOTALS		208 (33)*	10 da.-82 yr.

* General anesthesia (33 of 208 patients).

series for each dog. As nearly as possible, identical films in (a) right atrial-right ventricular (early dextro) filling phase, (b) dextro and pulmonary arterial filling phase, and (c) levo filling phase were selected from each of the 8 angiocardigraphic studies on a given dog. The 8 films of each phase were matted together and compared visually with one another. Figure 5 is a typical example of the comparative densities of the 8 different radiopaque solutions for each of the three filling phases.

We observed a slightly distinguishable difference between the contrast resulting with Hypaque 50 per cent and Hypaque 90 per cent. No difference could be noted with Hypaque 90 per cent, Urokon 70 per cent, and Cardiografin 85 per cent. Renografin 76 per cent and Renografin 60 per cent produce apparently equal opacification density and cannot be distinguished definitely from Ditriakon and Renovist. In fact, it is quite difficult to be *certain* that there is any notable differ-

ence in opacification density throughout the entire group of 8 media. It is remarkable that in these studies, which closely simulate clinical selective catheter angiocardiology, there is so little over-all difference in the opacifications produced by these several radiopaque substances.

CLINICAL STUDIES

For a number of years we had employed both Diodrast 70 per cent and Urokon Sodium 70 per cent for our clinical intrathoracic cardiovascular opacification procedures. With the introduction of the diatrizoate compounds, we made a change to the high-concentration Hypaques and Cardiografin, both of which are diatrizoate formulae. In 1959, at a Conference on Radiopaque Diagnostic Agents under the auspices of the New York Academy of Science, one of us (J. S. L.) reported certain physical measurements of Hypaque 90 per cent, Hypaque 85 per cent, Cardiografin 90.5 per cent and Cardiografin 85

75 PER CENT, DITRIKON AND RENOVIST

Number of Injections and Dose Range

One Injection		Two Injections		Three Injections		Four Injections		Five Injections	
No. Patients	Dose Range (c.c.)	No. Patients	Total Dose Range (c.c.)	No. Patients	Total Dose Range (c.c.)	No. Patients	Total Dose Range (c.c.)	No. Patients	Total Dose Range (c.c.)
9	5-50	5	16-70
9	5-60	16	10-100	3	30-120	2	24-130
10	5-50	2	16-18
5	75-100
16	23-50	10	24-110	4	85-170	4	40-150
..	..	3	55-100	2	63-70
..	..	13	65-110	8	82-120	5	90-145
2	30-43	2	60-80	1	110
10	40-45	3	72-84	2	85-110
2	40-44	1	135
4	40-50
3	35-45
..	..	25	65-95	3	100-118	6	125-156
..	..	3	68-90
..	..	3	44-90	2	132-136
..	..	3	65-90	1	92	3	119-143
..	2	82-86	1	187
70	5-100	88	10-110	27	30-170	22	24-156	1	187

per cent, along with the results of our clinical experiences with these media in 287 examinations. The reported studies included cardiac ventriculography, suprasternal thoracic aortography, selective catheter angiocardiology, and catheter thoracic aortography. The incidence of reactions was recorded (22). In the past two years, we have been using the somewhat less concentrated and less viscid Ditrakon, Renovist, and Hypaque 75 per cent for 208 intrathoracic cardiovascular opacification procedures. These latter opaque media have been adapted to ten different types of procedure or combinations of procedures. Hypaque 75 per cent was employed on 14 occasions, Ditrakon on 31, and Renovist on 163.

Table V-A is a summation of the types of examination, the radiopaque solution used, the number of patients and their age ranges, the number of injections, and the dosage ranges. The number and extent of reactions are listed in Table V-B.

It will be noted that on occasion a fairly high total dosage was administered, the maximum being 187 c.c., involving 5 injections. It is difficult or almost impossible to compare accurately the number, type, and degree of reaction produced by these three radiopaque agents. We have the general impression that the incidence of reactions is about the same for all and that the degree of such reactions is very similar. We are, however, of the distinct opinion that the reactions are definitely less marked as compared with our previous experiences with the more concentrated diatrizoate media. Our most extensive experience has been with Renovist, and we have not hesitated to employ multiple injections or higher dose levels than we considered advisable with the more concentrated diatrizoate media. We have certainly been impressed that the reactions are decidedly less marked with Renovist than with Diodrast 70 per cent and Urokon 70 per cent. We also believe that the diatrizoate

TABLE V-B: INCIDENCE OF REACTIONS WITH HYPAQUE

Procedure	Radiopaque Medium	Heat			Nausea			Vomiting		
		Slight	Mod- erate	Se- vere	Slight	Mod- erate	Se- vere	Slight	Mod- erate	Se- vere
Selective Catheter Angiocardiography	Hypaque-M 75%	3	5
	Renovist	7	6	..	1
	Ditriakon	3	4
Venous Abdominal Aortography	Renovist	1	4
Catheter Thoracic Aortography	Renovist	7	23	..	3	1
	Ditriakon	2	3	..	1
Coronary Arteriography	Renovist	8	18
	Ditriakon	..	5	1
Cardiac (Catheter) Ventriculography—Left	Renovist	3	12	..	3	1	..
	Ditriakon	1	2
Cardiac (Needle) Ventriculography—Left	Renovist	2	2
	Ditriakon	1	2	..	1	1
Cardiac (Catheter) Ventriculography—Left/Catheter Thoracic Aortography	Renovist	7	27	..	2	3	1	1
	Ditriakon	1	2	..	1
Selective Catheter Angiocardiography/Catheter Thoracic Aortography	Renovist	2	2
Selective Catheter Angiocardiography/Cardiac (Catheter) Ventriculography—Left	Renovist	3	3	1
Selective Catheter Angiocardiography/Cardiac (Catheter) Ventriculography—Left/Catheter Thoracic Aortography	Renovist	2	1
TOTALS		53	121	1	12	4	1	3	1	..

* One occasion of mild convulsion, with complete recovery.

† One occasion of apnea, 30 seconds duration.

media, particularly the solutions of somewhat lower concentration, have a considerably wider margin of safety than do Urokon and Diodrast.

The relative ease of injectability is a decided advantage of these lower-concentration diatrizoate solutions as compared with those of higher concentration. We are not, however, impressed that there is any remarkable reduction in the effectiveness of opacification of the cardiac chambers or intrathoracic great vessels as compared with our studies using the more highly concentrated agents. It is our opinion that the ability to inject the required dose more rapidly compensates for the difference in iodine content.

DISCUSSION

A true evaluation of the relative merits

of different cardiovascular radiopaque media is difficult. Such an analysis must take into account the physical properties of the solutions and particularly the facility with which they can be injected in adequate amount within a short period of time. A critical appraisal must also be concerned with the radiodensity of the respective media and, most certainly, with the number and degree of undesirable reactions.

In present-day clinical cardiovascular opacification procedures, relatively small-bore catheters are commonly utilized. At times and under certain conditions it is necessary to employ catheters as small as F5 and F6 and, in these circumstances, rapid delivery of an adequate dose of the opaque agent becomes a problem. An effective pressure injection apparatus is a

ITH HYPAQUE

	Omitting	
	Moderate	Severe
1	0.00	0.00
2	0.00	0.00
3	0.00	0.00
4	0.00	0.00
5	0.00	0.00
6	0.00	0.00
7	0.00	0.00
8	0.00	0.00
9	0.00	0.00
10	0.00	0.00
11	0.00	0.00
12	0.00	0.00
13	0.00	0.00
14	0.00	0.00
15	0.00	0.00
16	0.00	0.00
17	0.00	0.00
18	0.00	0.00
19	0.00	0.00
20	0.00	0.00
21	0.00	0.00
22	0.00	0.00
23	0.00	0.00
24	0.00	0.00
25	0.00	0.00
26	0.00	0.00
27	0.00	0.00
28	0.00	0.00
29	0.00	0.00
30	0.00	0.00
31	0.00	0.00
32	0.00	0.00
33	0.00	0.00
34	0.00	0.00
35	0.00	0.00
36	0.00	0.00
37	0.00	0.00
38	0.00	0.00
39	0.00	0.00
40	0.00	0.00
41	0.00	0.00
42	0.00	0.00
43	0.00	0.00
44	0.00	0.00
45	0.00	0.00
46	0.00	0.00
47	0.00	0.00
48	0.00	0.00
49	0.00	0.00
50	0.00	0.00
51	0.00	0.00
52	0.00	0.00
53	0.00	0.00
54	0.00	0.00
55	0.00	0.00
56	0.00	0.00
57	0.00	0.00
58	0.00	0.00
59	0.00	0.00
60	0.00	0.00
61	0.00	0.00
62	0.00	0.00
63	0.00	0.00
64	0.00	0.00
65	0.00	0.00
66	0.00	0.00
67	0.00	0.00
68	0.00	0.00
69	0.00	0.00
70	0.00	0.00
71	0.00	0.00
72	0.00	0.00
73	0.00	0.00
74	0.00	0.00
75	0.00	0.00
76	0.00	0.00
77	0.00	0.00
78	0.00	0.00
79	0.00	0.00
80	0.00	0.00
81	0.00	0.00
82	0.00	0.00
83	0.00	0.00
84	0.00	0.00
85	0.00	0.00
86	0.00	0.00
87	0.00	0.00
88	0.00	0.00
89	0.00	0.00
90	0.00	0.00
91	0.00	0.00
92	0.00	0.00
93	0.00	0.00
94	0.00	0.00
95	0.00	0.00
96	0.00	0.00
97	0.00	0.00
98	0.00	0.00
99	0.00	0.00
100	0.00	0.00

§ One occasion of grande mal convulsion, 5 minutes duration, with complete recovery.

§ One occasion of grande mal convulsion, 5 minutes duration, with complete recovery.

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chambers or vessels provide the most satisfactory type of study. Selective placement of the catheter in locations within the intrathoracic cardiovascular system, where a bolus injection will provide the maximal opacification of structures of clinical interest, is the type of procedure which can produce the most accurate diagnostic information. In such instances, multiple injections in several catheter locations may be necessary.

The foregoing remarks may not seem pertinent to an evaluation of cardiovascular radiopacifying media. Nonetheless, it is the opinion of the authors that these considerations are of greater importance than comparatively minor differences in iodine content of the radiopaque media. Relevant considerations are the toxicity of the media, their injectability, and the incidence

and degree of reactions. In our judgment, such associated factors as catheter type, size and length, pressure injection, and injection rate are more important than minor differences in absolute radiodensity of various media in the performance of selective catheter angiocardiology and related procedures.

The technical considerations of catheter positioning, rapid serial filming or cine-filming, the amount of injected medium, the technic of injection in the most favorable catheter locations for the most informative study, are matters which we consider to be of more significance than small variations in iodine content of the several cardiovascular radiopaque agents.

SUMMARY

Viscosity, catheter flow rates, and densitometry of the several radiopaque media commonly used for intrathoracic cardiovascular opacification procedures have been studied.

In controlled angiocardiology in dogs there appeared to be only slightly discernible differences in the density of cardiac opacifications produced by eight different radiopaque media of varying iodine content.

Animal tolerance studies indicate that the diatrizoate compounds are less toxic than the iodopyracet (Diodrast 70 per cent) or acetrizate (Urokon 70 per cent) compounds.

Certain factors which are considered to be of greater importance than minor variations in iodine content of contrast media are discussed in relation to effecting the most satisfactory cardiovascular opacification studies.

The combination of relatively easy injectability, comparatively low toxicity, moderate radiodensity, and a possible lower incidence and degree of undesirable reactions appears to favor those contrast media containing a moderate rather than a high concentration of diatrizoate compounds. This combination, particularly the lower toxicity, definitely favors these moderate-concentration diatrizoate solu-

tions over the lower-viscosity but more toxic iodopyracet (Diodrast 70 per cent) and acetrizate (Urokon 70 per cent) media.

The apparent relative safety of injection of larger total doses of the diatrizoate contrast media is considered.

Clinical experiences, especially the incidence and extent of untoward reactions observed in intrathoracic cardiovascular opacification studies with Hypaque 75 per cent, Ditiokon, and Renovist, are tabulated. The authors are favorably impressed with the over-all infrequency of undesirable reactions with these media.

The widest experience in this series has been with a recent preparation, Renovist. It is the authors' opinion that this diatrizoate medium, of moderate iodine content, effective radiodensity, comparatively low viscosity, and good flow rate through catheters appears to be one of the most satisfactory cardiovascular contrast preparations they have employed.

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REFERENCES

1. BASSETT, R. C., ROGERS, J. S., CHERRY, G. R., AND GRUHIT, C.: The Effect of Contrast Media on the Blood-Brain-Barrier. *J. Neurosurg.* 10: 38-47, January 1953.
2. BLOOR, B. M., WRENN, F. R., JR., AND MARGOLIS, G.: An Experimental Evaluation of Certain Contrast Media Used for Cerebral Angiography: Electroencephalographic and Histopathological Correlations. *J. Neurosurg.* 8: 585-594, November 1951.
3. BLOOR, B. M., WRENN, F. R., JR., AND MARGOLIS, G.: Effect of Intracarotid Iodopyracet (Diodrast) upon Cerebral Blood Flow. *Arch. Neurol. & Psychiat.* 71: 358-361, March 1954.
4. BROADBRIDGE, A. T.: Hypaque in Cerebral Angiography. A Clinical Assessment of Its Merits in Relation to Sodium Acetrizate (Diaginal) and Diodone. *Brit. J. Radiol.* 29: 577-584, November 1956.
5. BROMAN, T., AND OLSSON, O.: The Tolerance of Cerebral Blood-Vessels to a Contrast Medium of the Diodrast Group. An Experimental Study of the Effect on the Blood-Brain-Barrier. *Acta radiol.* 30: 326-342, 1948.
6. BROMAN, T., AND OLSSON, O.: Experimental Comparison of Diodonum with Sodium Acetrizate with Reference to Possible Injurious Effects on the Blood-Brain Barrier. *Acta radiol.* 46: 346-350, July-August 1956.
7. BROMAN, T., AND OLSSON, O.: Technique for the Pharmacodynamic Investigation of Contrast Media for Cerebral Angiography. Effect on the Blood-

- Brain Barrier in Animal Experiments. *Acta radiol.* 45: 96-100, February 1956.
8. DOTTER, C. T., WETCHLER, M. S., AND STEINBERG, I.: Contrast Substances for Angiocardiology: Study of Side Effects. *Radiology* 60: 691-698, May 1953.
 9. FADEM, C., AND LYONS, H. A.: Concentrated Hypaque Sodium for Angiocardiology: Preliminary Report. *Radiology* 70: 732-735, May 1958.
 10. FINBY, N., POKER, N., AND EVANS, J. A.: Ninety Per Cent Hypaque for Rapid Intravenous Roentgenography. Preliminary Report. *Radiology* 67: 244-245, August 1956.
 11. FISCHER, H. W., AND ECKSTEIN, J. W.: Comparison of Cerebral Angiographic Contrast Media by Their Circulatory Effects: An Experimental Study. *Am. J. Roentgenol.* In press.
 12. FOLTZ, E. L., THOMAS, L. B., AND WARD, A. A., JR.: Effects of Intracarotid Diodrast. *J. Neurosurg.* 9: 68-82, January 1952.
 13. GASS, H. H., AND JACOBSON, S. D.: The Use of Urokon in Cerebral Angiography. A Preliminary Report. *Am. J. Roentgenol.* 69: 428-432, March 1953.
 14. GREITZ, T. A.: Radiological Study of Brain Circulation by Rapid Serial Angiography of Carotid Artery. *Acta radiol. Suppl.* 140, 1956, pp. 5-20.
 15. GUZMAN, S. V., AND WEST, J. W.: Cardiac Effects of Intracoronary Arterial Injections of Various Roentgenographic Contrast Media. *Am. Heart J.* 58: 597-607, October 1959.
 16. INGVAR, D. H., AND SÖDERBERG, U.: Cerebral Vasomotor Tone and EEG During Injections of Ubradil. An Experimental Study with a New Method. *Acta radiol.* 47: 185-191, March 1957.
 17. KÄGSTRÖM, E., LINDGREN, P., AND TÖRNELL, G.: Changes in Cerebral Circulation During Carotid Angiography with Sodium Acetrizoate (Triurol) and Sodium Diatrizoate (Hypaque). An Experimental Study. *Acta radiol.* 50: 151-159, July-August 1958.
 18. KÄGSTRÖM, E., LINDGREN, P., AND TÖRNELL, G.: Circulatory Disturbances during Cerebral Angiography. An Experimental Evaluation of Certain Contrast Media. *Acta radiol.* 54: 3-16, July 1960.
 19. KENAN, P. D., TINDALL, G. T., MARGOLIS, G., AND WOOD, R. S.: The Prevention of Experimental Contrast Medium Injury to the Nervous System. *J. Neurosurg.* 15: 92-95, January 1958.
 20. KNOEFEL, P. K.: The Nature of the Toxic Action of Radiopaque Diagnostic Agents. *Radiology* 71: 13-14, July 1958.
 21. LAFIA, D. J., AND JAEGER, R.: Renografin as a New Contrast Medium for Cerebral Angiography: Report of Animal Experiments. *Radiology* 69: 398-400, September 1957.
 22. LEHMAN, J. S.: High Concentrations of Diatrizoate Methylglucamine. *Ann. New York Acad. Sci.* 78: 943-955, July 2, 1959.
 23. LEMCKE, W.: Erfahrungen mit Urografen "Scherer" in der zerebralen Angiographie. *Fortschr. a. d. Geb. d. Röntgenstrahlen* 82: 504-505, April 1955.
 24. LEWITAN, A., AND KROOP, I. G.: Experience with Two New Media in Angiocardiology. A Preliminary Report. *Am. J. Roentgenol.* 82: 779-783, November 1959.
 25. LINDGREN, P.: Carotid Angiography with Triiodobenzoic Acid Derivatives. Comparative Experimental Study of the Effects on the Systemic Circulation in Cats. *Acta radiol.* 51: 353-362, May 1959.
 26. LINDGREN, P., AND TÖRNELL, G.: Blood Circulation During and After Peripheral Arteriography. Experimental Study of the Effects of Triurol (Sodium Acetrizoate) and Hypaque (Sodium Diatrizoate). *Acta radiol.* 49: 425-440, June 1958.
 27. LINDGREN, P., AND TÖRNELL, G.: Blood Pressure and Heart Rate Responses in Carotid Angiography with Sodium Acetrizoate (Triurol). An Experimental Study in Cats. *Acta radiol.* 50: 160-174, July-August 1958.
 28. LINDNER, D. W., MARTIN, F. A., WEBSTER, J. E., AND GURDJIAN, E. S.: An Evaluation of Hypaque Sodium (Win 8308-3) for Cerebral Angiography. *S. Forum* 7: 553-559, 1956.
 29. MASSELL, T. B., HERINGMAN, E. C., AND GREENSTONE, S. M.: An Evaluation of Newer Opacification Media: Diatrizoate and Diprotrizoate. *Arch. Surg.* 78: 293-299, February 1959.
 30. MASSELL, T. B., GREENSTONE, S. M., AND HERINGMAN, E. C.: Evaluation of Diatrizoate (Hypaque) in Peripheral Angiography and Aortography. *J.A.M.A.* 164: 1749-1752, Aug. 17, 1957.
 31. MCCHESENEY, E. W., AND HOPPE, J. O.: Studies of the Tissue Distribution and Excretion of Sodium Diatrizoate in Laboratory Animals. *Am. J. Roentgenol.* 78: 137-144, July 1957.
 32. NESBIT, R. M., AND MORROW, J. W.: Clinical Experiences in Excretory Pyelography. A Comparative Study of Different Contrast Media (Hypaque 50%, Miokon 50% and Urokon 50%) in 3,454 Cases. *Am. J. Roentgenol.* 82: 849-852, November 1959.
 33. PENDERGRASS, H. P., TONDREAU, R. L., PENDERGRASS, E. P., RITCHIE, D. J., HILDRETH, E. A., AND ASKOVITZ, S. I.: Reactions Associated with Intravenous Urography: Historical and Statistical Review. *Radiology* 71: 1-12, July 1958.
 34. SANDSTRÖM, C.: Contrast Media for the Kidneys, Heart and Vessels, and Their Toxicity. *Acta radiol.* 39: 281-298, April 1953.
 35. SCHMIDT, H. W.: The Behaviour of the Pial Vessels During and After the Intracarotid Injection of Roentgen Contrast Media. *Acta radiol.* 44: 100-108, August 1955.
 36. SEAMAN, W. B., AND SCHWARTZ, H. G.: Cerebral Arteriography with Sodium Acetrizoate (Urokon Sodium) 30%. *Arch. Surg.* 67: 741-745, November 1953.
 37. STEINWALL, O.: An Improved Technique for Testing the Effect of Contrast Media and Other Substances on the Blood-Brain Barrier. *Acta radiol.* 49: 281-284, April 1958.
 38. TATELMAN, M., AND PAKUSCH, R. S.: A Comparative Evaluation of the Newer Contrast Media for Excretory Urography. *Radiology* 70: 238-241, February 1958.
 39. TINDALL, G. T., KENAN, P. D., PHILLIPS, R. L., MARGOLIS, G., AND GRIMSON, K. S.: Evaluation of Roentgen Contrast Agents Used in Cerebral Arteriography. II. Application of a New Method. *J. Neurosurg.* 15: 37-44, January 1958.
 40. WHITELEATHER, J. E., AND DESAUSSURE, R. L.: Experience with a New Contrast Medium (Hypaque) for Cerebral Angiography. *Radiology* 67: 537-543, October 1956.

(Pro le summario in interlingua, vider le pagina sequente)

SUMMARIO IN INTERLINGUA

Un Evalutation de Substantias de Contrasto Cardiovascular

Esseva studiate le viscositate, le rapiditate del fluxu intracatheteral, e le comportamento densitometric de plure medios de radio-opacitate que es in uso commun in procedimentos de opacification cardiovascular intrathoracic.

In angiocardioraphia a controllo in canes, solmente micre differentias esseva discernibile in le densitates del opacification cardiac producite per octo differente medios con varie concentrationes de iodo. Studios de tolerantia in iste animales indicava que le compositos diatrizoatic es minus toxic que le compositos iodopyracetic (Diodrast, 70 pro cento) o acetrizoatic (Urokon, 70 pro cento).

Le combination de (1) un relativemente facile injicibilitate, (2) un comparative mente basse toxicitate, (3) le moderate radiodensitate, e (4) un possibilemente reduce incidentia e grado de reactiones adverse pare favorar le substantias de contrasto que contine un moderate concentration de compositos diatrizoatic in supra del medios a iodopyraceto (Diodrast, 70 pro cento) e a acetrizoato (Urokon, 70 pro cento) con lor plus basse viscositate sed plus forte toxicitate.

Es presentate in forma tabular le ex-

perientias clinic—specialmente le incidentia e le grado del reactiones adverse observate in studios a opacification cardiovascular intrathoracic—con Hypaque de 75 pro cento, Ditrion, e Renovist. Le autores es favorabilemente impressionate per le infrequentia de reactiones adverse que es associate con le uso de iste medios.

Le experientias le plus extense in le presente serie ha concernite le recentemente introduce preparato, Renovist. Le autores ha trovate que iste medio a diatrizoato, con su moderate contento de iodo, su efficace radiodensitate, su comparative basse viscositate, e su bon comportamento de fluxu in le catheter, es un del plus satisfacente preparatos de contrasto cardiovascular que illes ha unquam empleate.

Es opinate que le considerationes technic del positionamento del catheter, del rapiditate del expositiones serial o cinematic, del quantitate de substantia injicite, e del methodo de injection in le situs catheteric le plus favorable pro le plus informative studio possibile es plus significative que le micre variationes in le contento de iodo inter le varie agentes de radio-opacitate cardiovascular.



Intercalative Angiography

Cardiovascular Spot-Filming¹

ROBERT J. BOUCEK, M.D.,² WILLIAM P. MURPHY, JR., M.D., and FRANCISCO A. HERNANDEZ, M.D.³

INTERCALATIVE angiography is the electronically controlled spot-filming of an opacified portion of the cardiovascular system. This form of angiography differs from the selective angiography described by Jönsson *et al.* (1) and by Lind *et al.* (2) in that the injection of the medium and x-ray exposure are programmed by the electrocardiogram. The electronic sequence is activated by the R-wave of the electrocardiogram, which is recognized by a specially designed cardiac programmer, which discriminates between the P- or T-waves. A refractory period is inserted so that the discharge impulse is delivered at the desired millisecond after the R-wave. This discharge impulse then either initiates a rapidly acting injector or passes through a second timing device which trips off the x-ray exposure. This apparatus was designed for coronary arteriography but has widespread application for other selective angiography techniques.

Intercalative angiography obviates most of the limitations of the standard cardiovascular x-ray procedures. Because the volume of the injected radiopaque material is small, the injection time is shortened and there is therefore a discrete localization of the substance at the selected site. In addition, the electronically controlled and highly selective x-ray exposure eliminates unnecessary radiation.

The purpose of this report is to describe the apparatus and record the experiences gained from its application, the method of procedure, and the characteristics of cardiovascular spot-filming which approach the ideal.

INSTRUMENT CHARACTERISTICS

(a) *Cardiac Programmer*: The development of the cardiac programmer began

more than four years ago in our laboratories and made possible the study reported by Casten *et al.* (3). Further developments and modifications have been made since that initial report. This instrument synchronizes injection of the opaque medium with x-ray triggering. The R-wave of the electrocardiogram provides the initiating trigger. This trigger first fires a one-shot multivibrator that has a long enough recovery time to prevent refiring before the next QRS complex. Simultaneously, a scaler circuit is initiated to provide output pulses for every two or four waves. A "count-down" of every wave from one to four can therefore be obtained.

A second trigger, in series with the first, is activated by the specified wave. Following this second trigger there is a variable delay circuit which can be preset from 0.01 to 1.5 seconds. After this delay, a similar circuit fires to provide a signal, adjustable within the range of 0.01 to 1.5 seconds, which in turn biases two output thyatrons. These provide power to a solenoid valve, which in turn activates the hydraulic injector piston.

(b) *Injector*: The hydraulic injector is designed for high-speed injection and convenience of operation. It is entirely self-contained and motor-driven with a continuously operating pump. The oil recirculates and may be used an indefinite number of times. All components are designed to exceed the required pressure and speed performance.

The hydraulic system operates the injecting cylinder through a mechanical linkage, thus separating the system from the patient. The injecting cylinder is a thick-walled glass tube that permits observation of the clearance of air from the

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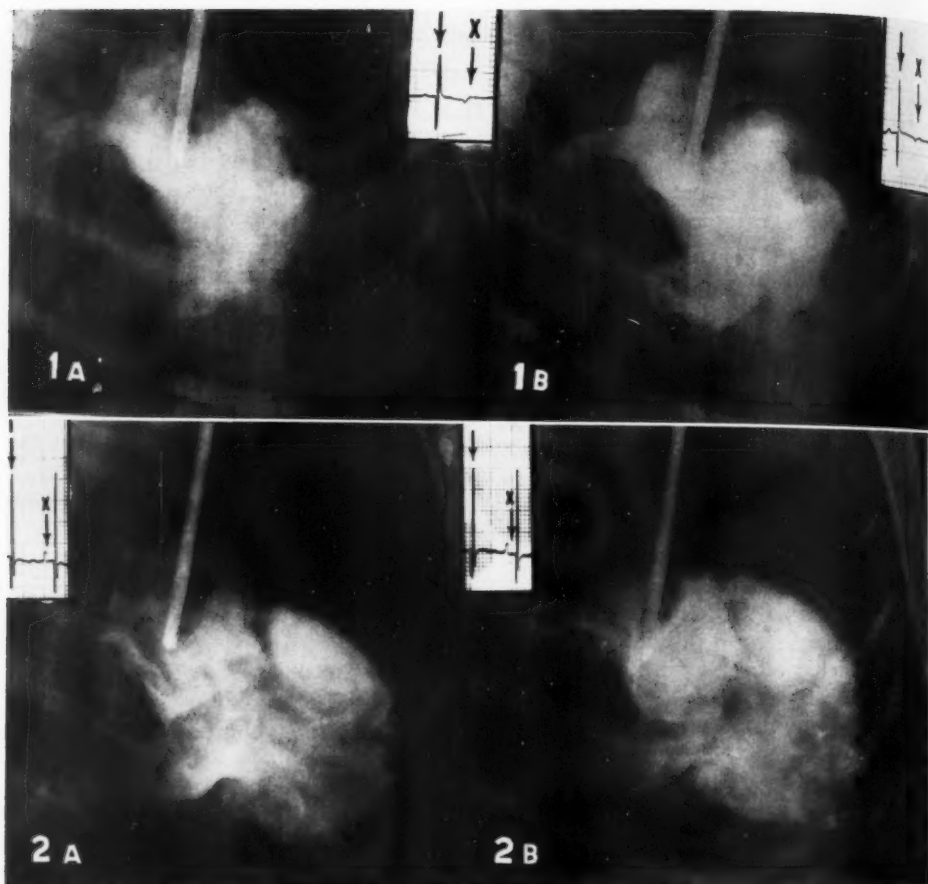


Fig. 1. Injection of 3 ml. of 70 per cent sodium acetrizoate (Urokon) into the right atrium of a dog (8 kg.).

A. Tricuspid valve opening.

B. Tricuspid valve opened; right ventricle filling.

Fig. 2. Injection of 3 ml. of 70 per cent sodium acetrizoate (Urokon) into the right atrium of a dog (8 kg.).

A. Right ventricle filled. Note leaflets of the tricuspid valve.

B. Right ventricle filled; atrial systole. Compare atrial size with A.

material to be injected. It holds a maximum of 41.5 ml. A simple mechanical linkage permits removal of the cylinder complete with its stainless steel end plates and piston for the purpose of steam sterilization.

The system consists of an electric motor-powered gear pump working from a 1-gallon reservoir. This pump forces oil into an hydraulic accumulator connected to a pilot-operated pressure regulator. The regulator permits recycling of the oil at a constant pressure. The accumulator pressure is transmitted to nitrogen con-

tained within a rubber bladder. The oil under pressure is held in place by a high-speed electrically operated valve controlled by the cardiac programmer. This valve delivers oil to the cylinder that drives the injecting piston.

The injecting cylinder is housed in an aluminum case containing a thermostatically controlled heating element that maintains the solution to be injected at the desired temperature.

(c) *X-ray Trigger*: The R-wave that initiates injection also initiates the x-ray trigger. Following a preset delay (0.01

to 3 seconds) in the x-ray triggering mechanism, thyatron circuits similar to those in the cardiac programmer fire. These energize the x-ray machine.

All of the modules are contained in a mobile console and are connected internally.

METHOD OF PROCEDURE AND RESULTS

Radiopaque substances used in this study were 90 per cent sodium diatrizoate (Hypaque) or 70 per cent acetrizate (Urokon).

(a) *Venous Angiography:* The catheter is advanced through a peripheral vein into a portion of the cardiovascular system. Because of the possibility of repositioning of the catheter by flailing, a blind-tip catheter with multiple holes located circumferentially around its end is used.

After the catheter is in place, the patient is positioned for the most favorable viewing. The catheter is then manually filled with the radiopaque substance. Predetermined injection and x-ray triggering times are set into the programmer. When everything is in readiness, the manual button is depressed and the instrument senses the next R-wave and activates the intercalative angiogram.

(b) *Arterial Angiography:* A blind-tip catheter is advanced through the right brachial artery unless the clavicle on the right side deforms the angle of the underlying subclavian artery, in which case the left brachial artery is used. Catheterization of the ascending aorta by this latter route is more difficult, however, as the current of blood flow favors passage into the descending aorta. For coronary angiography, the Lehman catheter is modified so that the efflux hole on the concave surface is $3/4$ inch from the tip. This is necessary to insure the passage of the radiopaque substance into the coronary ostium. The catheter is then passed into the ascending aorta and the tip lodged in a sinus of Valsalva. If both coronary arteries are to be visualized, the catheter tip is placed in the posterior noncoronary sinus. For individual right or left coronary artery

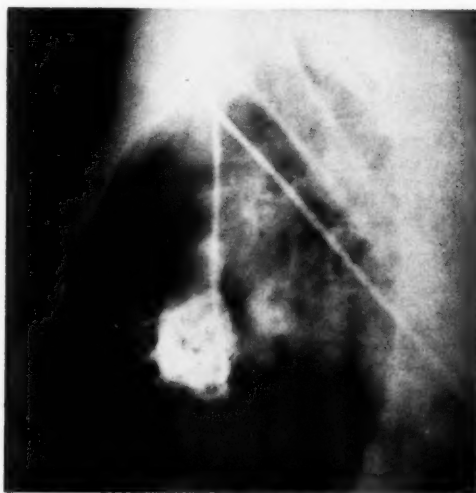


Fig. 3. Eisenmenger's complex in an adult female patient (left lateral position); 15 ml. of 90 per cent sodium diatrizoate (Hypaque). Right ventricle, at beginning of systole; note trabeculae and large outflow tract and the ventricular septal defect.

opacification, placement is in the respective sinus.

Programmed Venous Angiography

A. *Intercalative Angiograms:* (1) Right Atrium. The catheter was passed through a peripheral vein into the right atrium. The optimum injection time was immediately following the R-wave, when the tricuspid valve was closed. X-ray exposure was made with the T-wave.

(2) Right Atrium and Right Ventricle. The catheter was placed in the right atrium and injection was done immediately following the R-wave in all instances.

- (a) Opening of *tricuspid valve* (Fig. 1) visualized by x-ray exposure immediately following the T-wave.
- (b) *Right ventricle* (Fig. 2, A): x-ray exposure prior to the next P-wave.
- (c) *Atrial systole and right ventricle filling* (Fig. 2, B): x-ray exposure following the P-wave.
- (d) *Right ventricle with outflow tract* (Fig. 3): x-ray exposure just preceding the next R-wave.

The volume of sodium diatrizoate (Hypaque) required was as follows:

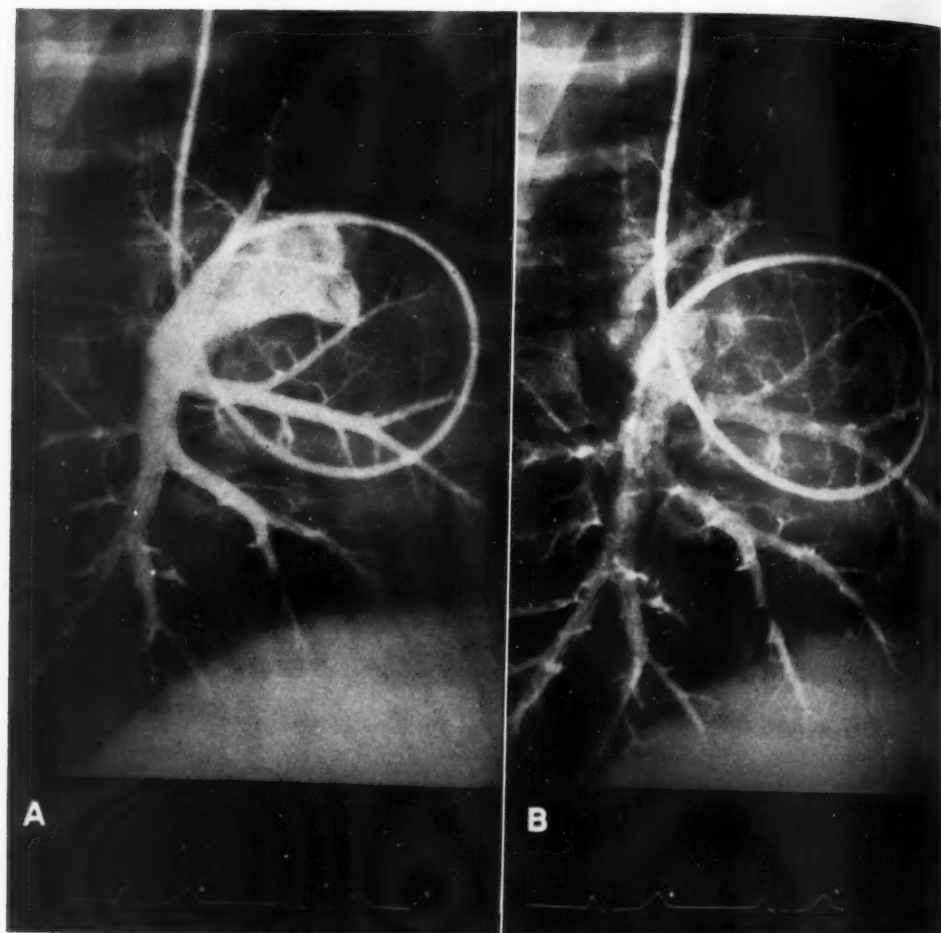


Fig. 4. Injection of 5 ml. of 70 per cent sodium acetrizate (Urokon) in a dog (25 kg.).
 A. Secondary divisions of the pulmonary arteries. Note pulmonary valve.
 B. Tertiary and quaternary divisions of the pulmonary arteries.

(a) Human beings:

Infants: not determined but should be similar to that used in the dog, *i.e.*, 2 to 3 ml.

Children: 3 to 7 ml.

Adults: 15 to 20 ml. without severe cardiomegaly; 25 to 30 ml. with cardiomegaly.

(b) Dogs (70 per cent sodium acetrizate (Urokon)):

Less than 10 kg. weight: 2 to 3 ml.

More than 10 kg.: 3 to 5 ml.

(3) Pulmonary Artery. The catheter was passed through the right side of the

heart and into the main pulmonary artery.

(a) Primary divisions of the pulmonary arteries: injection during the early phases of diastole (immediately following T-wave) with x-ray triggering in mid-diastole of the same cycle.

(b) Tertiary and quaternary divisions of the pulmonary arteries (Fig. 4): injection immediately after the R-wave with x-ray triggering at the end of the next mechanical systole.

The volume of sodium diatrizoate used was as follows:

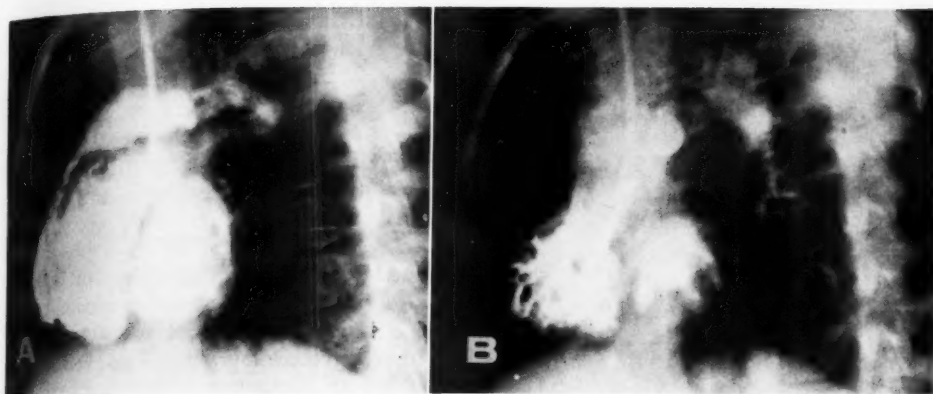


Fig. 5. Tetralogy of Fallot in a 5-year old boy (left lateral position); 5 ml. of 70 per cent sodium acetrizoate (Urokon).

A. Ventricular filling, right *via* injection, left *via* ventricular septal defect. Note infundibular stenosis.
B. Ventricular systole; simultaneous filling of aorta and pulmonary artery. Note the hypertrophied parietal band of crista supra-ventricularis and the hypertrophied trabeculae.

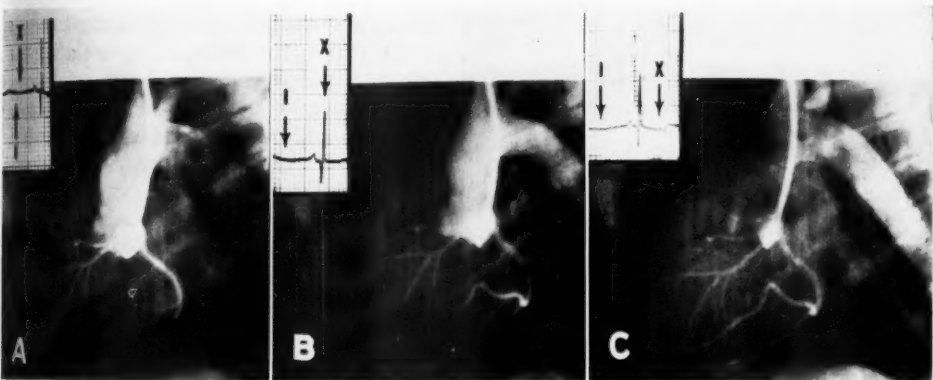


Fig. 6. Coronary arteriography (left lateral position) in a dog (10 kg.); 2 ml. 70 per cent sodium acetrizoate (Urokon).

A. Filling of the first portion of the left coronary artery.
B. Filling of the left coronary system.
C. Filling of the left coronary system and, in addition, the perforating secondary branches.

(a) Human beings:

Adults: 15 to 20 ml.

(b) Dogs:

Less than 10 kg. weight: 3 to 5 ml.

More than 10 kg.: 5 to 6 ml.

(B) *Programmed Injection with Rapid Film Changing*: In general, injection times and type of catheter were similar to those described for intercalative angiography. Visualization of the right ventricle and its outflow tract was the exception.

(1) *Anomalous Pulmonary Venous Drainage*: The catheter was placed in

either cava depending upon the area suspected of pulmonary venous drainage. Injection was made at the end of systole when the tricuspid valve is closed and the right atrium is nearly filled. The volume of opaque substance required for children was 1 to 3 ml.

(2) *Tetralogy of Fallot*. The catheter was placed at the high right ventricle position. Injection was made in early diastole, exciting a premature contraction (Fig. 5, A and B). The volume of opaque solution for children was 5 ml.



Fig. 7. Adult female patient (left lateral position); 12 ml. of 90 per cent sodium diatrizoate (Hypaque). Note diseased left anterior descending artery with normal right and circumflex arteries.

Programmed Arterial Angiography

Coronary Artery Visualization. The catheter was positioned as described above (page 567). The injection was made at the time of coronary artery filling, *i.e.*, the middle third of diastole. X-ray visualization of the primary divisions of the coronary artery was accomplished by triggering the exposure in the final third of diastole (Fig. 6, A). The secondary branches of the coronary arteries were seen on exposure at the time of the next R-wave (Fig. 6, B). Distal coronary branching was demonstrated by exposure at the end of the next mechanical systole (Fig. 6, C). The left anterior oblique position gave satisfactory visualization (Fig. 7). Anteroposterior views provided excellent visualization of the right coronary artery.

The volume of sodium diatrizoate used was as follows:

- (a) Human beings:
15 ml. caused no ECG changes with 25 injections in 14 patients.
- (b) Dogs:
2 ml. injection caused transient T-wave changes persisting for 4 to 6 beats.

DISCUSSION

Intercalative angiography or cardiovascular spot-filming requires the use of electronic devices which are activated by the electrocardiogram. This technic removes the vagaries of either rapid film-changing or the manual injection of a large amount of radiopaque material. Blurring of detail occurs with rapid film-changing (4 per second), with x-ray visualization dependent upon the chance recording of the exposure at the critical moment.

In order to perform intercalative angiography successfully, high-speed injections must be made so that the bolus of material will be imposed between or within a cardiac cycle. The hydraulic injector designed for this technic permits the delivering of adequate volumes of the opaque medium through an 80-cm. catheter in less than half a second for adults and in approximately one- to two-tenths of a second for children. With a knowledge of the physiology of blood flow, the course of the injected material can be predicted and accurately filmed.

By the discrete positioning of a small bolus of the radiopaque material, the usual flooding of the area to be filmed is avoided. This permits sharp definition of such fine structures as the interior of the ventricular cavity (Figs. 2, A and 4, B).

In addition, because of the small amounts of radiopaque material required, as many as four injections have been made during a single examination. No untoward reactions have occurred.

The sharp reduction in x-ray exposure which results from this technic is of great importance, particularly in pediatric angiocardiology. Not only is the radiation hazard diminished for the patient but it

is also reduced significantly for the examiner and technicians.

Modifications of the cassette are now being made so that four separate electronically programmed x-ray pictures can be taken with a single injection. This will increase the versatility of cardiovascular spot-filming, permitting a timed visualization of a dynamic event. This photographic stopping of rapid movement is accomplished without sacrifice of detail and should serve most of the requirements of angiography.

It appears that the majority of cardiovascular examinations can be carried out by intercalative angiography. In some instances, particularly for the dynamics of flow through the small vessels such as the coronary or cerebral, cineangiography with image intensification appears to have unique advantages of its own. Certainly, the indiscriminate x-ray exposure associated with rapid film-changing devices will no longer be necessary.

CONCLUSIONS

Injection into the cardiovascular system of a small volume of opacifying substance within milliseconds and subsequent spot-filming form the basis of "intercalative angiography." The procedure has the following advantages:

(a) The small amount of medium eliminates flooding of surrounding structures and superimposition of shadows.

(b) Repeat injections may be made during one examination.

(c) Injection is selectively made *via* a catheter introduced into the area to be visualized.

(d) Electronically programmed x-ray exposure reduces the random nature of x-ray viewing associated with the rapid film-changing technic.

(e) Programmed x-ray exposure reduces the radiation dose to the patient and to the examiner.

(f) This type of cardiovascular spot-filming reduces blurring of detail and gives extremely sharp x-ray definition.

No untoward complications have attended the use of hydraulic injection in 75 examinations.

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REFERENCES

1. JÖNSSON, G., BRODÉN, B., and KARNELL, J.: Selective Angiocardiography. *Acta radiol.* **32**: 486-497, December 1949.
2. LIND, J., BOESEN, I., and WEGELIUS, C.: Selective Angiocardiography in Congenital Heart Disease. *Progr. Cardiovas. Dis.* **2**: 293-314, January 1960.
3. CASTEN, G. G., MURPHY, W. P., JR., and ALLEY, J. C.: Augmentation of Diastolic Arterial Pressure by Mechanical Means: Effect on Coronary Sinus Flow. *Circulation* **16**: 866, November 1957.

SUMMARIO IN INTERLINGUA

Angiographia Intercalative: Filmation Cardiovascular a Spot

Angiographia intercalative es le electronicamente regulate filmation de spot de un portion opacificate del systema cardiovascular. Le injection del medio de contrasto e le exposition de radios X es programme per le electrocardiogramma. Un mechanismo de injection hydraulic permette rapidissime injectiones del medio de

contrasto con le ejection de adequate quantitates ab un catheter de 80 cm de longor in minus que un medietate de un secunda in adultos e in duo decimos de un secunda in juveniles. Nulle complication resultava del uso de iste injector in 75 studios.

Le avantages del angiographia intercalative es discutate.

Diagnostic Criteria of Basilar Impression¹

VINCENT C. HINCK, M.D., CARL E. HOPKINS, Ph.D., and BHIM S. SAVARA, D.M.D.

FOR TWENTY years it has been apparent that the diagnosis of basilar impression depends primarily on radiological evaluation. The anomaly is often missed clinically either because it is asymptomatic or because it presents deceptive signs and symptoms. The fact that numerous methods of measurement have been suggested for the radiological diagnosis indicates the complexity of the problem. The purpose of this article is to discuss various diagnostic criteria in the light of information now available.

DEFINITION

Briefly, basilar impression (or basilar invagination) is a deformity of the osseous structures at the base of the skull in the region of the foramen magnum. The perioraminal components of the occipital bone, and later the petrous portions of the temporal bones, are invaginated upward in such a manner as to diminish the volume of the posterior cranial fossa. Because of the relative immobility of the tentorium cerebelli above, there may result compression of the contents of the posterior fossa and the high cervical spinal cord, embarrassment of circulation, or impairment of the flow of cerebrospinal fluid.

Basilar impression may be congenital or it may be acquired as a result of diseases which cause malacic changes of the osseous structures around the foramen magnum. Paget's disease and osteogenesis imperfecta are relatively common causes of the acquired variety. Abnormalities of the central nervous system and adjacent osseous or soft-tissue structures may be associated, and signs and symptoms relating to these may result in a misleading symptom complex. The clinical findings have led too frequently to the incorrect diagnosis of

multiple sclerosis, syringomyelia, or other degenerative disease of the central nervous system, with the result that all thoughts of possible surgical amelioration are abandoned and the patient is considered incurable.

REVIEW OF LITERATURE AND CRITIQUE

McGregor, in 1948, reviewed the historical development of measurements for diagnosing basilar impression (12). Most of the earlier methods which he described have fallen into disuse. Chamberlain's line, on the other hand, is still widely used despite the fact that subsequent investigations have shown it to be relatively unreliable.

There are, at present, seven diagnostic methods which can be considered worthy of comment. They are summarized in Figures 1-3.

McRae's line and the digastric line seem to be the only two criteria which have weathered the storm of subsequent critical analysis.

McGregor's base line and Bull's angle use facial structures to define their lines of reference. In so doing they ignore the fact that the facial and neural components of the skull can develop quite differently and that, consequently, variations in the position and plane of the hard palate can lead to false readings. Bull's angle, in addition, has been shown to vary significantly with flexion and extension (1).

Although it is not a system of measurement, *McRae's line* does provide a valid foundation upon which to base one's judgment as to whether or not invagination is present. It further assists in estimating how far dorsal the dens has traveled relative to the foramen magnum and, therefore, how much the high cervical

¹ From the Department of Radiology and Department of Biostatistics, University of Oregon Medical School, and the Child Study Clinic of the University of Oregon Dental School, Portland, Ore. Aided by a grant from the Medical Research Foundation of Oregon, Inc. Some of the material used in this investigation was collected as part of a study of face growth that received partial financial support from Research Grants D-934 (R1) and D-934 (R1C1) from the National Institute of Dental Research, U.S.P.H.S. Accepted for publication in August 1960.

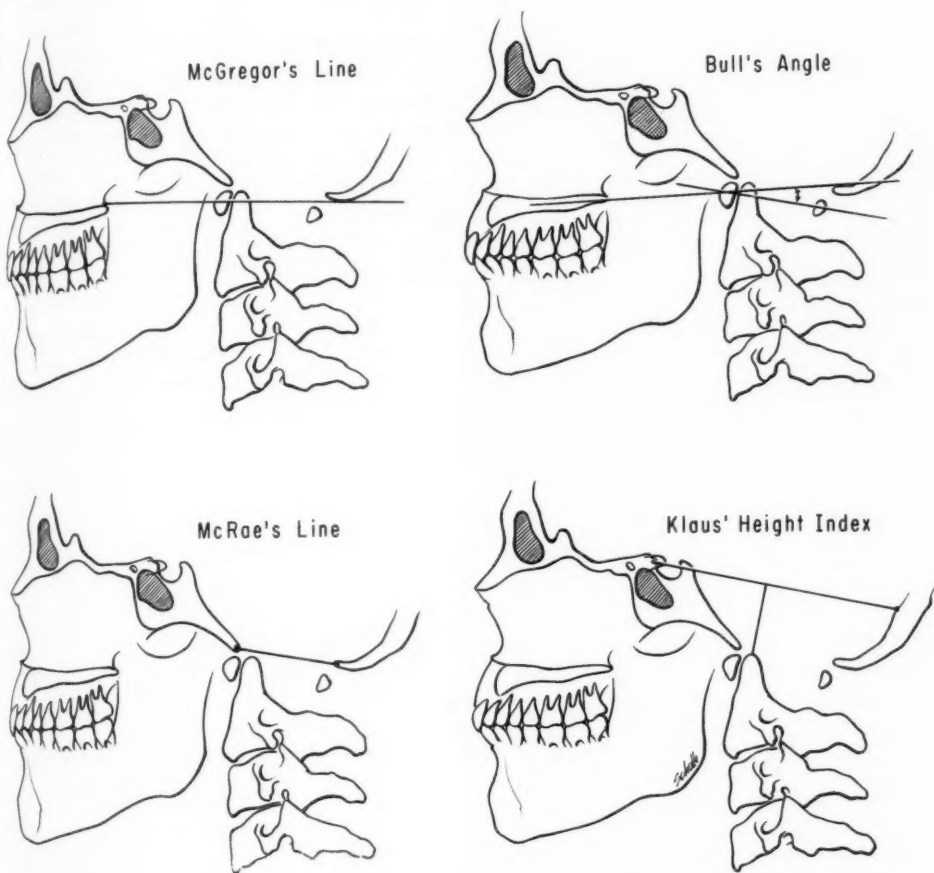


Fig. 1. *McGregor's base line*: A line from the posterosuperior aspect of the hard palate to the lowermost point on the midline occipital curve. According to McGregor, the apex of the dens should not rise more than 4.5 mm. above this line (12).

Bull's angle: A line along the plane of the hard palate intersects a second line along the plane of the atlas, subtending an angle (arrows) which does not normally exceed 13° (2).

McRae's line, or the *foramen magnum line*. A line from the ventral border of the foramen magnum (basion) to the dorsal border (opisthion). "If the line of the occipital squama is convex upward or if it lies above the line of the foramen magnum, basilar impression is present" (14). In addition, a perpendicular drawn from the apex to the reference line should intersect it in its ventral quarter. Otherwise neurologic disturbances can be expected (3).

Height index: A reference line from the tuberculum sellae to the highest point on the internal occipital protuberance. A second line (the height index) perpendicular to the first extends to the apex of the dens. It normally measures 40 or 41 mm., with a proportionately large variation. Values between 36 and 30 mm. reflect a "tendency toward" basilar impression while lower values are diagnostic (11).

spinal canal has been compromised. This, in turn, reflects the degree of probability of cervical cord injury by odontoid pressure (see legend, Fig. 1).

While *Klaus' height index* avoids the use of facial structures in the construction of reference lines, his normal values show a wide range. This casts doubt upon the merit of the measurement.

The *bimastoid line* has been supplanted

by the *digastric line*. The mastoid processes vary considerably in length from one individual to another. The normal position of a reference line based on these structures is therefore quite variable.

As previously indicated, the *digastric line* is drawn between the two digastric grooves. These lie in the lateral part of the base of the skull, that part which is not subject to displacement in the proc-

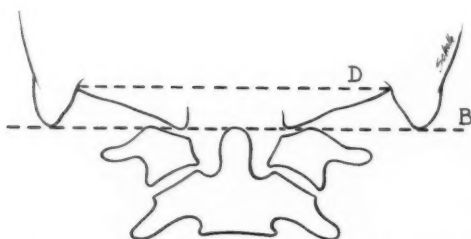


Fig. 2. *Bimastoid line*: The line (B) is drawn between the tips of the mastoid processes. Normally it should cross the atlanto-occipital joints. According to Fischgold (3) the odontoid apex should lie an average of 2 mm. above this line with a range between 3 mm. below and 10 mm. above.

Digastric line: The line (D) is drawn between the two digastric grooves which lie just medial to the bases of the mastoid processes. According to Fischgold, the distance measured from this line to the middle of the atlanto-occipital joints is normally about 10 mm. and decreases with invagination (6).

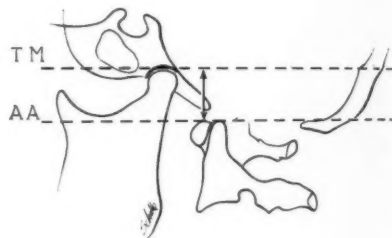
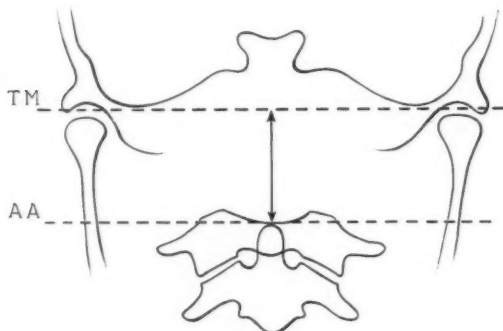


Fig. 3. *Temporomandibular line*: The distance is measured between two parallel lines, one (TM) at the level of the temporomandibular joints and one (AA) at the superior margin of the anterior arch of the atlas. Either an anteroposterior or lateral projection may be used. These lines are normally about 30 mm. apart with a range from 22 to 39 mm. The distance is diminished in basilar invagination (7, 8).

ess of basilar impression. This fact recommends the digastric grooves as reference points for assessment of invagination deformity.

The distance, as originally described, is measured from the digastric line to a line across the middle of the atlanto-occipital joints (6). Potential error introduced by the variable length of the dens is thereby obviated.² The normal distance of about 10 mm. is reduced in the presence of invagination (Fig. 4).

² Measurement of 65 films from the research file of normal lateral cervical spines disclosed a mean odontoid length of 17 mm., with a range extending from 12 to 22 mm.

It should be noted that bisection of the atlanto-occipital joints is not always accurate because, unlike the articulations between the lateral masses of the atlas and axis, the margins of the joints are often not very clearly defined.

Though it has only recently been described, the *temporomandibular line* is probably no improvement over its predecessors. Both the temporomandibular joints and the anterior arch of the atlas lie in or near the same coronal plane, slightly rostral to the atlanto-occipital articulations. In addition, the temporomandibular joints lie 20 or 30 mm. above these articulations. In contrast, the digastric grooves are in the same plane with and much closer to

the joints. Since the atlanto-occipital joints are the pivotal center for flexion and extension of the skull, it can be presumed that the temporomandibular joints will move more than the digastric grooves with change of skull position. It follows that values derived from measurements using the temporomandibular line will be more sensitive to changes caused by flexion and extension. When one considers the difficulty with which the so-called "true neutral" position is attained radiographically, the sensitivity of a reference point to flexion and extension becomes important.

The roentgenograms collected for the

present investigation do not permit study of the temporomandibular measurement. For the reasons mentioned, however, it is suggested that the temporomandibular line should not be considered an improvement over the digastric line without further study.

In summary, most of the diagnostic systems seem to be of dubious value. McRae's line and the digastric line appear to be the best. Despite its limitations, the authors feel that McGregor's base line is the most satisfactory available system for measurement on the lateral film. None of the methods which use the dens or the atlanto-occipital joints has excluded the error introduced by variability in length of occipital condyles among individuals.

The authors agree with McRae that, in view of anatomic variations, no measurement will be sufficiently sensitive to identify the mild case of invagination with assurance. Most or all methods are capable of giving an occasional false suggestion of invagination in the normal (13). Nonetheless, for those who are not very familiar with the normal radiographic anatomy of the occipito-cervical region, the diagnosis of basilar impression can be difficult even when the deformity is somewhat advanced. In such circumstances, even a moderately accurate system of measurement will serve a useful purpose as a general diagnostic guide.

PRESENT INVESTIGATION

The present investigation was directed at determining the values for McGregor's base line and Fischgold's digastric line as measured on an apparently normal sample of our population. These two lines were selected because they seem to represent the best measurements for diagnosing basilar impression on lateral and anteroposterior radiographs respectively.

Since basilar impression may be a congenital lesion and since there are no figures available for the normal range of values of the digastric and base lines in children, both children and adults were



Fig. 4. The digastric line demonstrated in a patient with basilar impression. Note that the atlanto-occipital joints and the apex of the dens lie well above the reference line. The atlanto-axial joints lie directly below the line. The base of the skull follows an abnormal upward course when traced from the digastric grooves toward the mid-line.

included in this investigation. All measurements were made with a radiographic measuring device accurate to the nearest tenth millimeter. Only films of satisfactory quality were included.

ACCURACY OF MEASUREMENT

Substantial inherent inaccuracy previously encountered in other film measurements (10) prompted us to turn attention first to determination of the accuracy of measurement of the various diagnostic criteria for basilar impression. By accuracy is meant closeness to the "true" value, or the average value that would be obtained if the measurement were to be independently repeated a large number of times.

The procedure for estimating the accuracy was as follows. A random selection was made of N films from the available supply. These films were carefully measured by Observer A (V.C.H.) and the data were recorded. They were then shuffled, their code identifications were changed, and new measurements were made the next day by the same observer. These two independent, blind measurements by the same observer provide an

estimate of the "within observer" error, or the inherent inaccuracy of measuring a film. This inaccuracy varies from film to film and is therefore averaged over the films thus measured, and expressed as a standard deviation,³ which simply represents the average amount of variability to be expected in repeat measurements of a film by the same observer. This variability will be called the *measurement error*.

Variability of different observers is estimated by independent repetition of the above procedure on the same film by a different observer. By comparing the readings of the two observers on each film, we obtain an estimate of average *overall inaccuracy*, which includes the measurement error as well as the variability of different observers. It is assumed that the observer error and the measurement error make independent contributions to the overall inaccuracy, and hence $s_{inacc}^2 = s_{observer}^2 + s_{meas}^2$. The inaccuracy and the measurement errors are estimated directly and the observer component is obtained by subtraction.

Accuracy determinations were made on measurements of the base line and of the digastric line, in adults and in children, with routine skull films, with laminagrams, or with both. The adult films were produced particularly for this study. The subjects were healthy medical students between twenty and thirty years old, mostly male, and tuberculosis hospital patients with no symptoms referable to the cervical spine, of various ages above twenty, male and female. The children's films were obtained from the files of the Child Study Clinic of the University of Oregon Dental School, which is conducting a current longitudinal study of apparently normal children, in which skull measurements are obtained at yearly intervals from age three to eighteen, by the Bolton-Broadbent Cephalometer.

The accuracy estimates are presented in

³ If d is the difference $X_1 - X_2$ between two repeat readings on a film, then the standard deviation of measurement is $s_{meas} = \sqrt{\sum d^2 / 2N}$, where N is the number of different films measured.

Table I, expressed as standard deviations and as "proportional errors," which are simply the standard deviation as a fraction of the mean value being measured. These errors appear to be normally distributed, so that, for instance, a proportional error of 85 per cent means that an average observer reading an average film will record a measurement within ± 85 per cent of the "true" value about two-thirds of the time, and within ± 170 per cent about 95 per cent of the time. For example, if the true value is 2.5 mm., the average observer has a two-thirds chance of obtaining as his measurement something between 0.4 and 4.6 mm. and is almost certain to record between -1.7 mm. and +6.7 mm.

It is notable that the overall errors for the different measurements, as shown in Table I, are all of about the same order of magnitude, 1.0 to 2.5 mm. When the distance being measured is small, as in the case of McGregor's base line, the proportional error may be very large. Conversely, when it is relatively large, as in the case of the digastric line, proportional error will be proportionally smaller.

Base Line, Adult, Routine Films: Out of 25 random films, 22 were measurable. These gave an overall mean measurement of 2.75 mm. The two observers showed a systematic difference in their measurements, Observer A averaging 2.10 mm. and B averaging 3.39 mm. The between observers error amounted to 44 per cent of the measurement. The measurement error was slightly higher for B (76 per cent) than for A (59 per cent) and on the average was higher (73 per cent) than the variability for observers. Taking into account both sources of error, the overall inaccuracy of a random film measured by a random qualified observer is seen to be 85 per cent.

Base Line, Adult, Laminagrams: On laminagrams the adult base line was measurable on 19 out of 20 films. The overall average base line measurement was -0.75 mm., with overall proportional inaccuracy 119 per cent.

TABLE I: ACCURACY OF BASILAR IMPRESSION MEASUREMENTS

	Mean Value of Measure- ment	Number of Films Measured	Variance (Square of S.D.) (mm. ²)	Standard Deviation (mm.)	Proportional Error (%)
A. Base line, adult, routine films (22 out of 25 measurable)					
Observer error	2.75	22	1.49	1.22	44
Measurement error: Observer A	2.10	22	1.53	1.24	59
Observer B	3.39	22	6.53	2.56	76
Avg. A + B	2.75	22	4.03	2.01	73
Overall inaccuracy	2.75	22	5.52	2.35	85
B. Base line, adult, laminagrams (17 out of 20 measurable)					
Observer error	-0.75	17	0.48	0.69	92
Measurement error: Observer A	-0.99	19	0.43	0.65	66
Observer B	-0.48	17	0.17	0.41	85
Avg. A + B	-0.75	18	0.30	0.55	73
Overall inaccuracy	-0.75	17	0.78	0.89	119
C. Base line, child, routine films (8 out of 10 measurable)					
Observer error	-1.38	8	2.90	1.70	123
Measurement error: Observer A	-0.54	10	Not repeated		15
Observer B	-1.95	7	0.084	0.29	
Avg. A + B	-1.38	7	0.084	0.29	21
Overall inaccuracy	-1.38	8	2.98	1.73	125
D. Digastric line, adult, routine films Accuracy determinations not done					
E. Digastric line, adult, laminagrams— to apex of dens: (20 measurable out of 20)					
Observer error			Not done		
Measurement error: Observer A	10.66	20	2.40	1.55	14.5
Observer B			Not done		
Avg. A + B			Not done		
Overall inaccuracy			Not done		
Digastric line, adult, laminagrams— to mid atlanto-occipital joint: (20 measurable out of 20)					
Measurement error: Observer A	12.19	20	2.35	1.60	13.1
F. Digastric line, child Pertinent anatomy of routine films is obscured in most instances. No laminagrams available for study.					
G. Effect of film quality on measurement inaccuracy—base line, adult, routine films					
Overall inaccuracy: Clear films		8	7.48	2.74	
Difficult films		6	5.64	2.38	

Base Line, Child, Routine Films: The base line was measurable on 8 out of 10 random films of children. A mean base line of -1.38 was obtained, with overall proportional inaccuracy 125 per cent. Here the observers were rather consistent within themselves, but showed large disagreements with each other, suggesting difficulty in defining what they were measuring.

Digastric Line, Adult, Laminagrams: Measurements of the digastric line, to the apex of the dens, were made on 20

selected measurable films and showed a modest proportional error of only 14.5 per cent. The observer error was not estimated, there being but one observer sufficiently trained to make these measurements. With measurements to the mid atlanto-occipital joint, the error was 13.1 per cent.

Digastric Line, Child: Obscure anatomy in the child made this measurement impossible on most of the routine films. No laminagrams were available.

The large inherent inaccuracy was

thought to be due primarily to difficulty of ascertaining the proper landmarks on a few of the films. To test this surmise both observers classified 22 medical student (routine) films into "clearly ascertainable," "difficult to ascertain," and "average." The overall inaccuracy was then determined for the 8 films considered quite unambiguous and the 6 considered very difficult by both readers. The results, surprisingly, show only a small difference in inaccuracy between the clear and the difficult films.

Standard Values

The standard adult values reported herein are based on single measurements to the nearest tenth of a millimeter made by one observer (V.C.H.). Each of these measurements is presumed to include three independent sources of variability: subject, observer, and measurement. The variance of these measurements should thus be the sum of the variances for the three sources, *i.e.*,

$$s^2 = s_{\text{subj.}}^2 + s_{\text{observ.}}^2 + s_{\text{meas.}}^2 = s_{\text{subj.}}^2 + s_{\text{inacc.}}^2$$

The overall inaccuracy of the measurements in Table I is generally of the same order of magnitude as the quantity being measured. For instance, with respect to McGregor's base line on the adult male skull film, the total variance is 10.96 sq. mm., based on measurement of 22 medical students and 24 tuberculosis hospital patients by a single observer. This 10.96 is the sum of 1.53 for the measurement (by this observer) plus 9.43 for biological variation of subjects.

If these standards are to be used by other observers, however, the observer variance estimated at 1.49 must also be added. The measurement error, averaged across observers, now becomes 4.03, giving an overall inaccuracy of 5.52 (Table I). This, added to the biological variation of 9.43, brings the total variance to 14.95, and tolerance should be based on this variance. The resultant tolerance limits (4) for 90 per cent of "normal" subjects, as measured by a random (qualified) observer, would be 0.33 ± 7.82 , or from -7.5 to $+8.2$

mm., a range so inflated by measurement inaccuracy as to render detection of minor anomalies quite unlikely. It may still, however, be useful for detection of moderate to severe impression, which is believed to produce measurements up to 15 or 20 mm.

One further warning must be entered before presentation of the normal values. Tolerance ranges are given for 90 per cent of "normal" subjects. A patient with measurements outside this range is thus rather unusual for a normal and should be suspect as abnormal—suspect rather than diagnosed, because this criterion still permits 10 per cent of "normals" (5 per cent on the high side only) to fall outside the range. What proportion of true abnormalities will be missed by this criterion (false negative diagnosis) can only be guessed. In order to determine the false negative probability, it would be necessary to have a series of definitive basilar impressions diagnosed on some other criterion.

McGregor's Base Line, Adult: The measurements were taken from 66 true lateral radiographs of the cervical spine and skull (T.F.D. 72 inches; patient sitting with head in neutral position; central beam directed at the level of C-2). Forty-two of the films were of in-patients at the tuberculosis hospital having no signs or symptoms referable to the high cervical spine or skull and 24 were of asymptomatic medical students and staff members. The subjects ranged in age from twenty-one to fifty-nine years.

The measurements derived from this series differ significantly ($P < 0.05$) from those of McGregor. The mean value for position of the apex of the dens was as follows: male subjects, 0.33 mm. above the line, with a standard deviation of 3.81 mm.; female subjects, 3.67 mm. above the line with a standard deviation of 2.62 mm. The average difference between male and female subjects was significant, being calculated as 3.06 mm. (Table II). In contrast, McGregor's mean value (combining both sexes) was 1.32 mm. below

the line with a standard deviation of 2.62 mm.

Despite the fact that our films were taken at T.F.D. 72 inches while McGregor's films were presumably taken at 40 inches, error based on the inverse-square law would be insignificant when dealing with a measurement difference to the order of 2 or 3 mm. On the other hand, racial differences may be partly responsible. McGregor studied African Bantus. He felt that he could apply his results directly to a Caucasian population because figures for the basal angle of the skull of his series closely approximated those of Brailsford, whose sample was Caucasian,⁴ and because his figures for Chamberlain's line closely matched those of Saunders (15), who was also working with Caucasians. These similarities notwithstanding, it seems ill-advised to use his figures without a comparable study on Caucasians.

The manner in which the patient was positioned for roentgenography probably accounts for part of the discrepancy. Our films were taken with the head and neck in true lateral projection. McGregor's radiographs were apparently taken with the patient prone and the head and neck rotated in order to obtain true lateral skull projection.

It has been established that, with rotation of the head, there is vertical approximation (telescoping) of the first cervical vertebra on the second (5). Since the roentgenograms of the patients in McGregor's series were obtained with the head rotated (his illustrations show this to be so) his figures should show a higher position for the dens than ours. The converse is true. This increases the likelihood of a racial difference.

Measurement on skull radiographs taken in the prone position introduces another possible source of error. Examination of a reasonably large series of such films will show that, when the skull is truly lateral,

TABLE II: MCGREGOR'S LINE: ADULTS (mm.)

	Medical Students	TB Hospital Patients	Pooled
Male			
N	22	24	46
Mean	0.14	0.50	0.33
Standard deviation (VCH)	3.37	3.24	3.31
Standard deviation (Random observer)	3.82	3.94	3.81
Female			
N	2	18	20
Mean	0.80	3.99	3.67
Standard deviation (VCH)	1.13	1.71	1.69
Standard deviation (Random observer)	2.30	2.63	2.62
Recommended Best Overall Estimates (by a Random Observer)			
	Mean	Standard Deviation	90% Tolerance Range for Normals (15)
Male subjects	0.33	3.81	-7.4 to +8.0 mm.
Female subjects	3.67	1.69	-2.4 to +9.7 mm.
Male-female average difference	-3.06*

Comment: There is evidently no significant difference between the two sources of subjects, but there is an appreciable difference according to sex. This difference is confirmed by a factorial analysis of variance, with correction for the extreme disproportionality in the subgroups.

* This best estimate of the mean difference is somewhat smaller than the apparent difference of 0.33-3.67, which is inflated by the disproportionality. The best unbiased estimate, -3.06, is obtained from the analysis of variance (16).

the neural arch of the atlas is often open. In those instances there must be lateral flexion as well as rotation in the occipito-cervical region. Exactly what effect this has on the measurement has not been determined.

In summary, there is a statistically significant difference between the figures in the two series. Technical factors probably account for a large part of the discrepancy, but there is reason to believe that racial differences also have some effect.

McGregor's Base Line, Child: Measurements were made independently (as they would be made by a diagnostic radiologist) on 258 films taken at yearly intervals on 43 normal children aged three to eighteen years. These children were being followed longitudinally in a Child Development Study at the University of

⁴Measurement of 76 skull radiographs in our series disclosed a mean value of 132° with a range from 118° to 147°. These figures are close to those of the other two observers.

Oregon Dental School. Since the collection of films for this purpose began only nine years ago, no single child has been followed for the full eighteen years. For radiographs, the child was seated with head in neutral position and the distance from the target to mid-sagittal plane of the head was 5 feet.

The plan was to determine standard normal values for children at each year

The statistical aspects of this problem have been considered in the references cited and need not be discussed here. The crux of the matter is that if, on the average, there is a substantial correlation between a child's measurements of one year and the next succeeding year, the correlation should be taken into account. This requires application of a statistical technique so cumbersome that, until the recent avail-

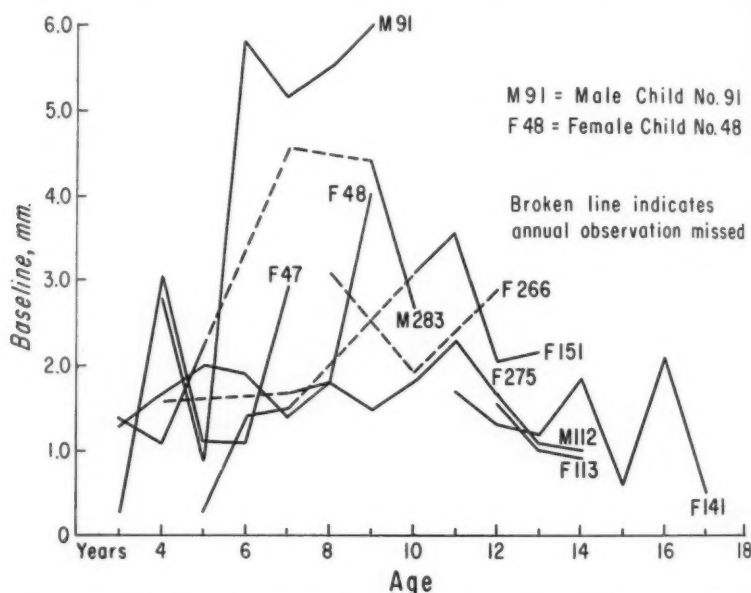


Fig. 5. Longitudinal base line measurements on ten random children from series.

of age from three to eighteen, based on about 10 children of each sex for each year. As in any longitudinal study, there were gaps and overlaps, presenting a special problem of mixed longitudinal sampling (9, 17). The purpose was to estimate mean values and tolerance ranges for the base-line measurement in childhood, taking age and sex into account.

Where the interest is in these yearly estimates, account must be taken of the fact that at each successive year we are using some of the same children over again to obtain our estimate of the norm for "all" normal children. Ordinarily, we would not expect these "same" children to vary as much as would "new" children.

ability of inexpensive electronic computing, it has seldom been used.

In our plan for analysis, we had provided for the electronic computation (courtesy of the Western Data Processing Center, U.C.L.A., Los Angeles, Calif.) needed to obtain the desired estimates. Preliminary screening of the data, however, confirmed what had already been adumbrated by our earlier studies of the errors of measurement of this dimension. The variations within the same child, from one year to the next, were large and random (see Fig. 5), indicating measurement difficulty rather than biological changes. Taking all the observations of all the children, the overall correlation between one year's

TABLE III: MCGREGOR'S LINE: CHILDREN
Summary of measurements (mm.)

Age (Years)	N	Male Mean	S.D.	N	Female Mean	S.D.	N	Male and Female Mean	S.D.
3	8	2.14	1.50	6	1.32	0.61	14	1.79	1.24
4	11	2.10	1.13	9	1.96	0.73	20	2.04	0.95
5	14	2.47	1.11	10	1.61	1.69	24	2.11	1.39
6	15	2.65	1.67	11	1.37	1.34	26	2.11	1.64
7	16	2.64	1.66	10	1.78	0.68	26	2.31	1.40
8	14	2.83	1.74	9	2.22	0.92	23	2.59	1.47
9	14	2.81	1.30	12	1.96	1.17	26	2.42	1.30
10	10	2.63	1.37	8	2.08	0.84	18	2.38	1.16
11	6	2.03	0.83	7	2.11	0.83	13	2.08	0.79
12	9	1.88	1.11	8	1.99	0.70	17	1.93	0.91
13	9	2.19	1.40	7	1.63	0.95	16	1.94	0.39
14	7	1.97	1.27	4	1.20	0.53	11	1.69	1.10
15	7	1.86	1.78	4	1.15	0.71	11	1.60	1.48
16	4	1.50	0.69	2	2.35	0.35	6	1.78	0.71
17	2	1.00	0.28	2	1.85	1.91	4	1.42	1.22
18	3	0.77	0.55	3	0.77	0.55

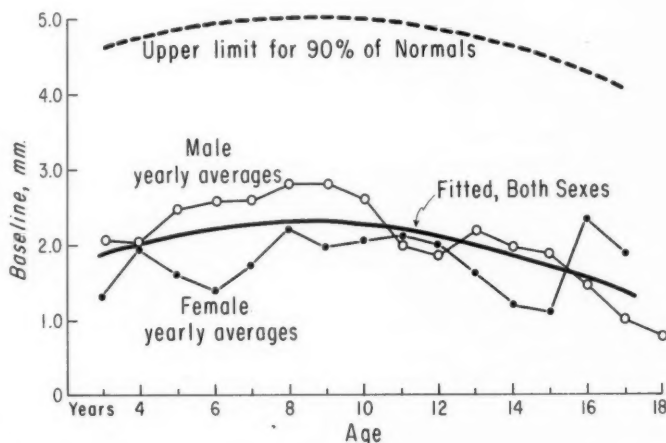


Fig. 6. Regressions of base line with age, with 90 per cent tolerance limit.

measurement and the next year's *on the same child* was calculated to be to the order of 0.4, which means that only $(0.4)^2$ or 16 per cent of the variance of measurements for the k th year is attributable to the measurement for the preceding year. When the correlation between successive measurements on the same child is as low as this, the complicated mixed longitudinal type of analysis does not give appreciably better estimates than the much simpler cross-sectional estimates that are so frequently used.

Hence we have used the cross-section type of analysis, even though the data were originally obtained longitudinally,

i.e., to estimate the mean measurement at age seven years, we simply use all of the children in this sample who were measured at seven years. For the eighth year mean we take all the children who were measured at eight years. Some of these are the same children and some are "new" children but since the correlation within the "same" child is so low they are statistically equivalent to "new" children, except for the possibility of bias arising from children who stay in the study year after year being different from children who are entering or being measured only once or twice. This bias can be serious in longitudinal growth studies of such visible measure-

TABLE IV: MCGREGOR'S LINE: CHILDREN
Fitted estimating line, with 90 per cent tolerance range,
both sexes

$$BL = 1.4 + 2.17A - 0.13A^2, \text{ S.E.} = 1.26 \text{ (mm.)}$$

Age	Mean Base Line	90% Tolerance Range*
3	1.94	-0.8 to 4.7
4	2.07	-0.7 to 4.8
5	2.17	-0.6 to 4.9
6	2.24	-0.5 to 5.0
7	2.29	-0.4 to 5.1
8	2.31	-0.4 to 5.1
9	2.30	-0.4 to 5.1
10	2.27	-0.5 to 5.0
11	2.21	-0.5 to 5.0
12	2.13	-0.6 to 4.9
13	2.01	-0.7 to 4.8
14	1.88	-0.9 to 4.6
15	1.71	-1.0 to 4.5
16	1.52	-1.2 to 4.3
17	1.31	-1.4 to 4.1
18	1.07	-1.7 to 3.8

* Ninety per cent of children similar to those of this sample are almost certain to lie within the range of Mean BL ± 2.2 (1.26).

ments as height and weight, in which case parental concern might well influence study faithfulness according as the child is seen to be progressing "normally" or otherwise. This kind of bias might also be different for the sexes, depending on the cultural values attached to normality and to extremes of height and weight. It is difficult to believe that such biases might be important in this case, since the children were followed for purposes of dental research rather than the more visible growth components. The motivation to continue in the study is thus assumed to be independent of the growth of the cervical spine and skull.

The means for each year and each sex, obtained by simple cross-section averaging, are given in Table III and illustrated in Figure 6. Up to the 10th year there appears to be a small difference between male and female means. In a much larger sample these differences could be adjudged real, but they are in the magnitude of 1 mm. or less and so, in the presence of both measurement and individual variation of substantially larger magnitude, they do not demand attention. Sex is therefore disregarded in the analysis.

Age means, as well as age for individuals, showed considerable instability (Figs. 5 and 6) and an apparent downward trend

toward maturity. A straight line failed to fit the age means [$F(1,256) = 1.97, P > 0.05$]. A parabola, however, fits adequately [$F(2,255) = 6.96, P < 0.001$], though with a quite large variation about the line (S.E. of estimate = 1.26 mm.). The equation is given in Table IV and illustrated in Figure 6.

This downward trend as maturity is approached is not very satisfying biologically, particularly in view of the findings of somewhat higher values for the adult female (see Table II). However, the curvature is slight and the variance around the line large, so that both the curvature and the discrepancy between the eighteen-year-old estimates and the adult sample could well be explained as a sampling artefact, with possibly a small contribution from the kind of bias mentioned above.

Until these age and sex effects can be more precisely elucidated with a much larger sample and/or greatly improved means of measurement, a reasonable summary of the practical situation would be: In 90 per cent of apparently normal children from three to eighteen years of age, of either sex, the apex of the dens is visualized about 2 mm. above the base line with a range from 0 to 5 mm.

Digastric Line, Adult: While Fischgold states that the digastric measurement is about 10 mm. (6), he makes no reference to the normal range of values. Accordingly, the mean and standard deviation were determined on 68 anteroposterior laminagrams of apparently normal adults. Of these, 45 were from the tuberculosis hospital research series and 23 from medical students and staff. (The 'aminagrams were taken with the patient supine and the skull positioned in such a way that the outer canthus of the eye and the external auditory meatus described a line perpendicular to the table top. T.F.D. was 40 inches.)

Two methods of digastric measurement were studied. The first, in the classical manner, measured the distance from the digastric line to the middle of the atlanto-

occipital joints. The second measured to the apex of the dens. We were interested in seeing how the two measurements compared, particularly since the dens is sometimes seen to better advantage than the atlanto-occipital joints in a given roentgenogram. For this comparison, observations were made on 51 tuberculosis hospital patients and 24 medical students and staff. The physical factors for radiography were as already described.

For the measurement to the atlanto-occipital joints the mean value was 11.66 mm., with a standard deviation of 4.04 (Table V). The measurement to the

TABLE V: DIGASTRIC LINE: ADULTS
Measured on Laminagrams to Atlanto-Occipital Joint (mm.)

	Medical Students	TB Hospital Patients	Pooled
N	23	45	68
Mean	12.01	11.49	11.66
Standard deviation (VCH)	2.70	3.71	3.40
Standard deviation (Random observer)*	3.48	4.31	4.04
Recommended Best Overall Estimate (by a Random Observer)			
Mean	11.66	4.04	3.8 to 19.5 mm.
Standard Deviation			90% Tolerance Range for Normals
Either sex	11.66	4.04	3.8 to 19.5 mm.

$t_{diff.} = 0.60$. Not significant.

* No direct estimate of between-observer inaccuracy was made for this measurement. Overall inaccuracy is accordingly guessed to be three times the measurement error of the single observer.

apex of the dens yielded a mean of 10.70 mm., with a standard deviation of 5.06 (Table VI).

Variation of values is primarily due to individual variation of the latero-medial slope of the base of the skull and the variation of the height of the occipital condyles. Measurement to the apex of the dens introduces the additional variable previously mentioned, namely, the length of the odontoid process.

The values derived from the measurement to the dens correspond more closely with Fischgold's original figures than do the measurements to the middle of the atlanto-occipital joint.

TABLE VI: DIGASTRIC LINE: ADULTS
Measured on laminagrams to apex of dens (mm.)

	Medical Students	TB Hospital Patients	Pooled
Male			
N	22	26	48
Mean	10.77	10.65	10.70
Standard deviation (VCH)	3.32	5.25	4.47
Standard deviation (Random observer)*	4.02	5.71	4.98
Female			
N	2	25	27
Mean	10.00	10.74	10.69
Standard deviation (VCH)	3.96	4.66	[4.64]
Standard deviation (Random observer)*	4.56	5.18	5.16
Male and Female			
N	75
Mean	10.70
Standard deviation (VCH)	4.53
Standard deviation (Random observer)*	5.06

Recommended Best Overall Estimate (by a Random Observer)

	Mean	Standard Deviation	90% Tolerance Range for Normals
Either sex	10.70	5.06	1.0 to 20.4 mm.

Comment: No significant differences appear in either sex or source of subjects.

* No direct estimate of between-observer inaccuracy was made for this measurement. Overall inaccuracy is accordingly guessed to be three times the measurement error of the single observer.

SUMMARY

The recent literature concerning criteria for the diagnosis of basilar impression has been reviewed. Various methods which are currently in vogue have been discussed in the light of information now available.

No measurement will be sufficiently sensitive to identify the mild case of invagination with assurance. Most or all methods are capable of giving an occasional false suggestion of invagination in the normal. Nonetheless, for those who are not very familiar with the normal radiographic anatomy of the occipito-cervical region, the diagnosis of basilar impression can be difficult, even when the deformity is somewhat advanced. In such circumstances, even a moderately accurate system of measurement will serve a useful purpose as a general diagnostic guide.

Measurement studies were undertaken to reassess normal values for McGregor's base line and Fischgold's digastric line since these seem to be the best measurements on the lateral and anteroposterior radiographs respectively.

It was found that the measurements for McGregor's base line are significantly different for the adult male and female. It was further noted that the measurements derived from the present investigation differ significantly from those of McGregor's series. Attempt has been made to account for the discrepancy.

The base line measurement has been studied in normal children. Problems relating to the establishment of a range of normal measurements are discussed.

With Fischgold's digastric line, the classical measurement (to a line crossing the middle of the atlanto-occipital articulations) as well as modification thereof (to the apex of the dens) were studied. Figures for both are included. The latter correspond fairly well with those of Fischgold.

Tolerance ranges which will include 90 per cent of "normal" subjects are given for each measurement as made by a random qualified observer.

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REFERENCES

1. BERGERHOFF, W.: Über die messtechnische Beurteilung der basillären Impression im Röntgenbild. *Zentralbl. f. Neurochir.* **18**: 149-162, 1958.
2. BULL, J. W. D., NIXON, W. L. B., AND PRATT, R. T. C.: Radiological Criteria and Familial Occurrence of Primary Basilar Impression. *Brain* **78**: 229-247, June 1955.
3. DECKER, K., FISCHGOLD, H., HACKER, H., AND METZGER, J.: Entwicklungsstörungen am atlanto-occipitalen Übergang. *Fortschr. a.d. Geb. d. Röntgenstrahlen* **84**: 47-57, January 1956.
4. DIXON, W. J., AND MASSEY, F. J., JR.: Introduction to Statistical Analysis. New York, McGraw-Hill, 2nd ed., 1957, p. 130.
5. FIELDING, J. W.: Cinerontgenography of the Normal Cervical Spine. *J. Bone & Joint Surg.* **39-A**: 1280-1288, December 1957.
6. FISCHGOLD, H., DAVID, M., AND BRÉCHAT, P.: La tomographie de la base du crâne en neurochirurgie et neuro-ophtalmologie. Paris, Masson & Cie, 1952.
7. FISCHGOLD, H., LIÈVRE, J. A., AND SIMON, J.: Indice radiographique de profil de l'impression basilaire. *Rev. du rhum.* **26**: 72-75, January 1959.
8. FISSORE, E.: Arc antérieur de l'atlas et articulations temporo-maxillaires dans l'impression basilaire. Paris, Thèse, 1958.
9. HENDERSON, C. R., ET AL.: The Estimation of Environmental and Genetic Trends from Records Subject to Culling. *Biometrics* **15**: 192-218, June 1959.
10. HINCK, V. C., AND HOPKINS, C. E.: Measurement of the Atlanto-Dental Interval in the Adult. *Am. J. Roentgenol.* **84**: 945-951, November 1960.
11. KLAUS, E.: Röntgendiagnostik der Platybasie und basillären Impression. Weitere Erfahrungen mit einer neuen Untersuchungsmethode. *Fortschr. a.d. Geb. d. Röntgenstrahlen* **86**: 460-469, April 1957.
12. MCGREGOR, M.: The Significance of Certain Measurements of the Skull in the Diagnosis of Basilar Impression. *Brit. J. Radiol.* **21**: 171-181, April 1948.
13. MCRAE, D. L.: The Significance of Abnormalities of the Cervical Spine. *Am. J. Roentgenol.* **84**: 3-25, July 1960.
14. MCRAE, D. L., AND BARNUM, A. S.: Occipitalization of the Atlas. *Am. J. Roentgenol.* **70**: 23-45, July 1953.
15. SAUNDERS, W. W.: Basilar Impression: The Position of the Normal Odontoid. *Radiology* **41**: 589-590, December 1943.
16. SNEDECOR, G. W.: Statistical Methods. Ames, Iowa, Iowa State College Press, 5th ed., 1956, p. 379.
17. TANNER, J. M.: Some Notes on the Reporting of Growth Data. *Human Biol.* **23**: 93-159, May 1951.

SUMMARY IN INTERLINGUA

Criteria Diagnostic de Impression Basilar

Impression basilar es un deformitate in que le componentes periforaminal del osso occipital—e plus tarde le portiones petrose del ossos temporal—es invaginate in alto in un tal maniera que le volumine del fossa postero-cranial es diminuite. Le condition escappa frequentemente al observation clinic, proque—de un latere—

illo pote remaner asymptomatic o—del altere—su signos e symptomatos es deceptive.

Le diagnose depende primarimente del evaluation radiologic. In lor studios in adultos e juveniles, le autores usava le linea de base de McGregor e le linea digastric de Fischgold in, respectivamente, le

roentgenogramma lateral e le roentgenogramma posterior pro establir valores normal.

Esseva trovate in 66 adultos que le mesuraciones normal basate super le linea de McGregor differeva significativamente inter masculos e femininas. Illos etiam differeva ab le mesuraciones del series original de McGregor mesme, possibilemente—al minus in parte—a causa de factores racial. Le mesuramentos del autores monstrava pro le distantia ab le linea de base usque al apice del dente un valor medie de 0,33 mm pro masculos normal (con un deviation standard de 3,81) e un valor medie de 3,67 mm in femininas normal (con un deviation standard de 2,62). In 68 subjectos, mesuraciones esseva effectuate pro le distantia ab le linea

de Fischgold usque ad un linea transversantele medietate del articulationes atlanto-occipital e usque ad le apice del dente. Le valores medie pro iste ultime mesuraciones esseva 10,70 mm pro masculos (con un deviation standard de 4,98 mm) e 10,69 mm pro femininas (con un deviation standard de 5,16 mm).

Le studios in 43 juveniles indicava le desiderato de un elucidation de certe effectos de etate e sexo super le base de plus extense series o de meliorate methodos de mesuration. Intertanto, un adequate summario del situation pare esser que in 90 pro cento del subjectos normal de etates de inter tres e dece-octo annos e del un o del altere sexo, le apice del dente es circa 2 mm in supra del linea de base, con un dispersion del valores ab 0 ad 5 mm.



Massive Neonatal Ascites¹

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FETAL OR NEONATAL ascites denotes an intraperitoneal accumulation of fluid during prenatal life or shortly after birth. Volumes under 100 c.c. may be clinically indiscernible (1); 200 c.c. is usually obvious by physical examination. Ascites of this greater degree not associated with generalized edema is of rare occurrence (18). Lord (16) in "over 8,000 infants" encountered only 2 examples.

HISTORICAL REVIEW

The earlier reports on fetal ascites appeared in the obstetrical literature and dealt primarily with dystocia resulting from the often massive abdominal enlargement. All the patients died in the perinatal period. The condition was briefly ascribed to and dismissed as congenital syphilis; this view was also expressed in the pediatric textbooks of that period. It was not until the end of the last century that the association of neonatal ascites with congenital anomalies was appreciated.

Fordyce (9), in 1894, collected 63 examples of fetal ascites, in which the most frequent finding was peritonitis. In 31 of these, visceral abnormalities were demonstrated. Such lesions as cirrhosis, hepatic gummata, anomalies of the lower intestinal and urinary tracts, suprarenal tumor, splenomegaly, and enlargement of the pancreas were described. Evidence of parental syphilis was found in only 9 of these 63 cases. Dorland (7) first differentiated "true fetal ascites" from "generalized anasarca" and abdominal swelling produced by visceral enlargement of various types. Of the 80 cases of true fetal ascites that he collected, about one-half were associated with peritonitis.

In more recent years, three large groups of underlying anatomical abnormalities have been implicated in the pathogenesis of ascites in the newborn: (a) intestinal



Fig. 1. Case I. Roentgenogram made at thirty minutes of life, in the supine position, showing marked distention of the abdomen, bulging of the flanks, and diffuse opacification. Gas is present in the esophagus, stomach, and proximal duodenum only. Surgery was performed shortly thereafter.

anomalies, especially perforation of the bowel secondary to malformation (2, 5, 8, 19, 26); (b) porto-hepatic abnormalities producing obstruction of the portal circulation (2, 4, 12, 17); (c) anomalies of the lower urinary tract. The importance of this last group was realized only during the last decade (10, 14, 16, 20). It also became apparent that the presence of massive abdominal fluid in the newborn carries a very grave prognosis, which may be improved with recognition and correction of the underlying anatomical aberration.

CASE PRESENTATIONS

Each of the cases described below is representative of one of the three main categories of malformation implicated in the pathogenesis of fetal ascites.

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CASE I (Gastrointestinal): A white, full-term female infant was born of a 20-year-old Rh-positive mother with a negative serologic test for syphilis. At birth, the infant was slightly cyanotic and dyspneic. The abdomen was grossly enlarged and numerous dilated superficial veins were present. Delivery was complicated by the great size of the abdomen.

Roentgenograms obtained about thirty minutes postpartum (Fig. 1) showed a markedly distended, homogeneously opacified abdomen with air present only in the stomach and proximal duodenum. Paracentesis yielded copious amounts of thick, yellowish fluid suggestive of meconium. The presence of intestinal perforation was assumed and laparotomy was immediately performed. Several loculations of fluid were found, walled off by tenacious brown material which firmly matted the bowel. A large perforation proximal to a 2-cm. atretic segment was present in the terminal ileum. This segment of the bowel was resected and an ileo-ascending colostomy was performed. The immediate postoperative course was uneventful, but incomplete small intestinal obstruction and urinary tract infection subsequently developed. Death resulted at the age of twenty-eight days, from peritonitis and overwhelming septicemia.

Autopsy revealed extensive focal meconium peritonitis with abscess formation and multiple adhesions.

CASE II (Porto-hepatic): A colored female infant was born about three weeks prematurely of a 29-year-old S.T.S.-negative, Rh-positive mother. The mother had been treated seven years previously for pulmonary tuberculosis. She had also received two courses of antisyphilitic therapy ten and five years earlier.

On admission, the infant weighed 1,510 grams and was not distressed. The abdomen was markedly enlarged, with a girth of 32 cm. The liver was questionably palpable and the spleen was about 3 cm. below the costal margin. There was no peripheral edema. Pertinent laboratory findings were a serum bilirubin of 4.8 mg. per cent, with a direct bilirubin of 1.8 mg. per cent. Blood culture and S.T.S. were negative. The stools and urine were unremarkable.

Paracentesis yielded a clear amber fluid which showed a count of 72 white blood cells with about 95 per cent mononuclears. The total and direct bilirubin levels were 2.8 and 0.9 mg. per cent, respectively. The protein was 5.8 gm. per cent. All bacteriological examinations of the blood and abdominal fluid were negative.

On admission films (Fig. 2), a greatly distended, fluid-filled abdomen was seen, with gas present in the stomach and proximal small bowel.

In view of the family history of tuberculosis and the character of the ascitic fluid, the infant was placed on antituberculous therapy. Vomiting,



Fig. 2. Case II. Roentgenogram obtained at about six hours of age, showing homogeneous opacification of the abdomen, with bulging of the flanks due to intra-abdominal fluid. Gas has progressed to the ileum without distention of the bowel.

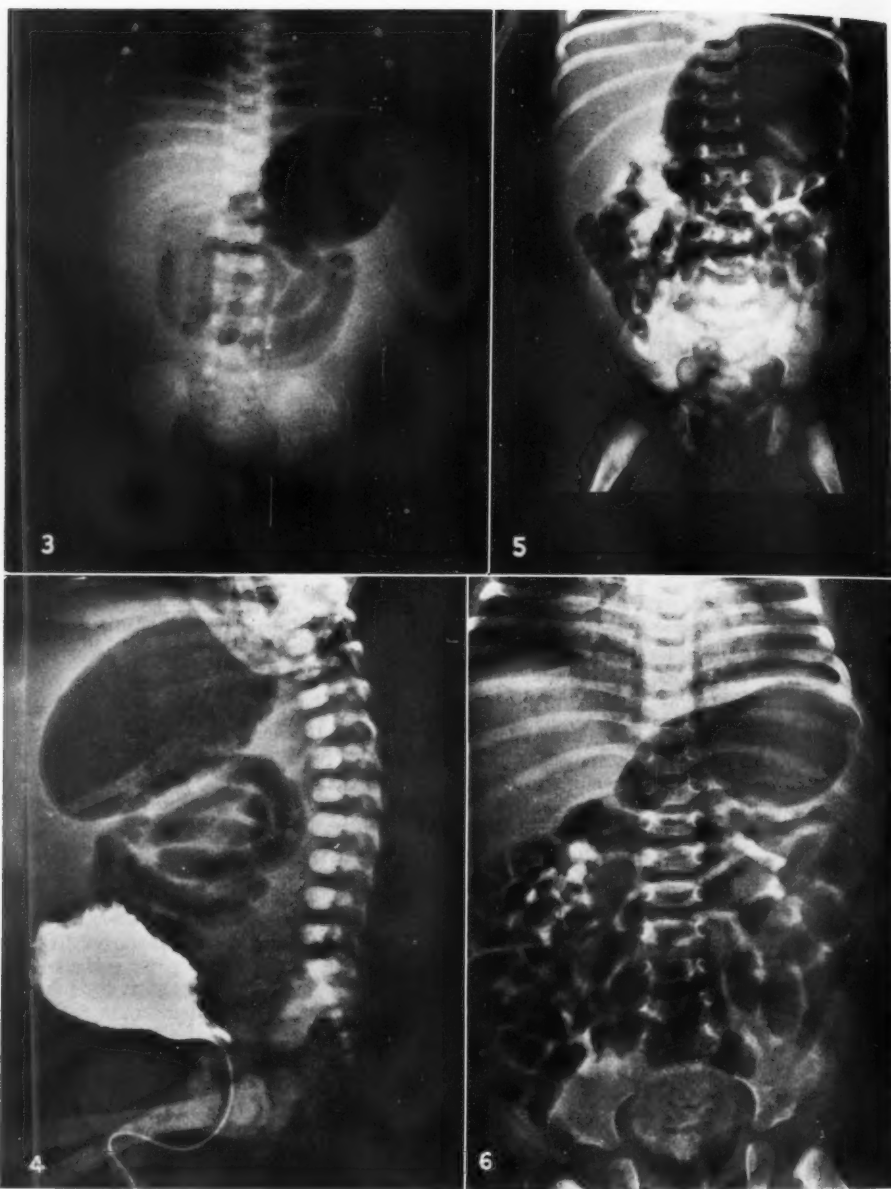
weight loss, lethargy, and episodes of apnea occurred, and the child's condition gradually deteriorated. Radiologic examination of the gastrointestinal tract disclosed no abnormality.

Subsequently, clinical jaundice appeared and the total and direct serum bilirubin rose to 20 and 18 mg. per cent, respectively. Biliary obstruction or atresia now seemed certain, and exploration was undertaken in the hope that a lesion amenable to surgical repair might be present. At operation, bile-stained ascitic fluid and a moderately enlarged liver, deep green in color, but without gross evidence of cirrhosis, were found. The gallbladder and a duct leading directly from it to the duodenum contained no bile. No other extrahepatic biliary channels could be identified. The infant tolerated the procedure poorly and expired shortly thereafter at twenty-four days of age.

At autopsy, apart from the extrahepatic atresia noted at surgery, intrahepatic biliary atresia and biliary cirrhosis were found.

CASE III (Genitourinary): A full-term white female infant was born of a 28-year-old Rh-positive mother whose serologic test for syphilis was positive. At birth, the abdomen appeared enlarged, and roentgenograms obtained at two and seven hours of life suggested the presence of fluid, with air only in the stomach. Reportedly, meconium stools were passed normally.

Previous to admission, the infant had apparently not voided. On admission, at the age of eighteen



Figs. 3-6. Case III

Fig. 3. Roentgenogram made in the supine position at eighteen hours of age, showing diffuse increase in density of the abdomen with distention due to fluid. The gas has progressed only to the mid small bowel without distention. The picture had not changed significantly at twenty-six hours of age.

Fig. 4. Cystogram. A lateral view at the age of twenty-six hours, showing a distended trabeculated urinary bladder indicating vesical neck obstruction.

Fig. 5. Intravenous pyelogram at four days of age. Maximal opacification two hours after injection and marked dilatation of the calyces and pelves, tortuous ureters, and distended urinary bladder.

Fig. 6. Intravenous pyelogram at four and a half months of age, showing satisfactory excretion at fifteen minutes and marked improvement as compared with Fig. 5.

hours, the abdomen was markedly distended, with a girth of 42 cm. and prominent superficial abdominal veins. Bowel sounds were present but decreased. Admission laboratory studies revealed a white blood count of 25,550, with an unremarkable differential count. Serum urea nitrogen was 44 mg. per cent, chlorides 92, sodium 123, and potassium 6.4 mEq/L respectively. Urine removed by catheterization was cloudy and brown and contained many red cells as well as a few white blood cells per high-power field. Blood and urine cultures showed no growth. Fluid removed by paracentesis was hemorrhagic and appeared xanthochromic after centrifugation; the specific gravity was 1.015, the hematocrit was 4 per cent, and the urea nitrogen level 41 mg. per cent. Chlorides were 91, sodium 116, and potassium 7.3 mEq/L, respectively.

Films of the abdomen (Fig. 3) at eighteen hours of age demonstrated diffuse opacification in the enlarged abdomen, with air present only in the stomach and proximal small bowel. The latter did not appear distended. Re-examination at twenty-six hours showed no distal progress of the gas. The barium-enema study disclosed a normal colon. A cystogram (Fig. 4) revealed a distended and trabeculated bladder, indicating the presence of bladder neck obstruction. There was no reflux into the ureters.

At operation, the peritoneal cavity contained a large amount of turbid fluid. The gastrointestinal tract appeared intact. The bladder was nodular, hypertrophied, and dilated; there was a sealed-off 3-mm. perforation in its dome. When the bladder was opened, the vesical outlet was found to be covered by a membranous flap, preventing the passage of a catheter from above; a catheter passed from below easily lifted this valve-like membrane which arose from the posterior surface of the bladder just above the vesical neck. This diaphragm was excised. On histologic examination, it revealed squamous metaplasia and muscular hypertrophy. Biopsy of the bladder wall also showed muscular hypertrophy, as well as edema and dilated vascular spaces.

An intravenous pyelogram three days after operation showed delayed excretion and marked bilateral hydroureter and hydronephrosis (Fig. 5). Subsequently, repeated urinary tract infections developed, but on a second intravenous pyelogram, five weeks later, there was marked decrease of the degree of pelvicalyceal and ureteral dilatation. The serum urea nitrogen remained within normal limits and the residual urine was only 5 c.c. The patient was discharged about two months after admission on appropriate antibiotic therapy. The third intravenous urogram, at the age of four and a half months, showed further improvement (Fig. 6). The infant was last seen at the age of eight months, when she appeared well developed and alert; her urinary tract infection was apparently in remission.

DISCUSSION

In most of the recorded cases of fetal or neonatal ascites the infants were either stillborn or died shortly after birth. In about 165 cases, there were only 4 survivals beyond the neonatal period (4, 13, 17, 24). In view of the serious prognosis, the importance of recognition and correction of the underlying malformation cannot be over emphasized. As indicated earlier, these malformations fall into three main groups:

(a) *Gastrointestinal Abnormalities:* Theoretically, the gastrointestinal abnormalities associated with neonatal ascites are amenable to surgical relief. The accumulation of large amounts of fluid usually occurs after perforation of a viscus secondary to atresia, stenosis, intussusception, volvulus, or intra- or extra-abdominal herniations (8). Other less frequent lesions cited include Meckel's diverticulitis and fetal appendicitis with rupture (2). Perforation of the bowel not associated with an underlying mechanical obstruction or a primary inflammatory process has been described (5, 8, 23, 26).

The presence of small amounts of fluid within the abdominal cavity does not necessarily indicate perforation and peritonitis, since transudation from the surface of obstructed bowel is possible; underlying perforation should be suspected when massive ascites is present. When large volumes of fluid are found at birth, the perforation must have occurred *in utero*, probably after peristaltic activity had begun. According to Boikan (5), this occurs about the fifth month of gestation. The presence or absence of calcification gives no definite clue to the duration of the perforation, since calcification can occur as early as twenty-four hours after rupture (5, 19). Initially, the peritonitis resulting from chemical and foreign-body irritation is sterile. After birth, however, following passage of bacterial organisms into the peritoneal cavity, a septic peritonitis may result; this compromises the outlook considerably. None of the 27 patients with

prenatal perforation of the bowel with ascites described in the literature, including our Case I, has survived. The majority were either stillborn or died within a few hours after birth.

Prompt surgical intervention may improve this poor outlook; however, lower intestinal tract surgery is prone to be followed by the development of adhesions (11), and, since the lower ileum is the most common site of atresia and perforation, the postoperative course is frequently complicated by bouts of partial obstruction and poor nutrition. Persistent peritonitis, progressing in spite of surgical closure and supportive chemotherapy, is an additional complication. This was present in our Case I.

(b) *Porto-hepatic Abnormalities:* Porto-hepatic anomalies are rarely amenable to surgical repair. Ascites is produced as a result of intra- and/or extrahepatic obstruction of the portal circulation. Extrahepatic obstruction is uncommon. It results from interference with the blood flow in the portal vein. An enlarged pancreas, a cyst of the right adrenal, and hypoplasia of the portal and splenic veins are mentioned as causes in earlier reports (9). Intrahepatic obstruction is found much more frequently and congenital hepatic cirrhosis is most commonly responsible.

It is now recognized that cirrhosis in the newborn is of two types: portal and biliary.

Ascites in *portal cirrhosis* has been described by Bellin (4). In his case, cirrhosis was considered secondary to maternal infectious hepatitis in the third trimester of pregnancy. Other causes cited included Wilson's hepatolenticular degeneration, hereditary angiomatosis, and cytomegalic inclusion disease.

Biliary cirrhosis is caused by obstruction of the bile flow as a result of intra- and/or extrahepatic atresia of the bile ducts. It is considerably more common than portal cirrhosis. According to Gross (11), "the only hope for cure lies in surgical exploration looking for the small percentage of cases in which it is possible to find some

situation which can be relieved by operative means." Complete intrahepatic atresia has an extremely poor prognosis.

Rare examples of intrahepatic obstruction are cystic degeneration of the liver (7), solitary cyst of the right lobe of the liver, and large hepatic gummata (21).

(c) *Genitourinary Abnormalities:* The frequent association of ascites with abnormalities of the lower genitourinary tract was noted as early as 1894 by Fordyce (9), largely on the basis of autopsy findings. In spite of this, the association of obstructive anomalies of the lower genitourinary tract in liveborn infants with ascites has only been recently stressed. Lord, in her comprehensive study, collected 18 cases in which dilatation of the urinary tract was found. In 16 of these, an obstructive lesion was described. She distinguished two types of lower urinary tract malformations associated with ascites.

The first type, of which there were 5 cases, consisted of imperforation of the anus associated with atresia of the urethra. The rectum usually terminated in a cul-de-sac behind a giant bladder or persistent urogenital sinus. Gross hydronephrosis was present and the volume of fluid in the bladder was often greater than the amount of ascitic fluid. Such combined malformations have an extremely poor prognosis.

The second type is characterized by isolated urethral obstruction. There were 11 infants, all males, in this group. Most of these were stillborn, and the cases were recorded because of the obstetrical problem they presented. Urethral obstruction of this type in males is produced by paired, flaring, membranous flaps arising from the verumontanum and attached to the anterior and lateral walls of the urethra. It is possible to pass a catheter upward, but outward flow of urine is impeded. A diaphragm-like membrane extending completely over the lumen, anywhere in the posterior urethra, not related to the verumontanum, can produce a similar obstruction. Hypertrophy and distention of the bladder wall and consequent uretero-hydronephrosis will result. To our knowl-

TABLE I: URETHRAL OBSTRUCTION IN LIVEBORN INFANTS WITH NEONATAL ASCITES

Author	Sex	Onset of Symptoms	Urinary Stream	Lesion	Survival
James	M	3 weeks	Normal	Posterior urethral obstruction	Alive and well at 8 months
Lord	M	5 weeks	Normal	Urethra not examined	Died at 6 weeks
	M	At birth	One drop at birth	Valve at verumontanum	Died at 1 1/2 hours
France and Back	M	6 1/2 weeks	Normal	Valve at verumontanum	Died at 7 weeks
	M	At birth	Anuria	Urethral valve. Bladder perforation	Died at 7 weeks
Parrott	M	8 days	Normal	Posterior urethral valve	Died at 28 days
Authors' case III	F	At birth	Anuria	Vesical neck valve. Bladder perforation	Alive and well, 8 months

edge, with the exception of our Case III, there is no record of urethral obstruction in a female infant born alive with neonatal ascites. Only 6 have been recorded in liveborn males (Table I).

Other rare causes of ascites in the newborn female infant described are Dorland's 2 cases of "fluid distention of the genital tract," due to agenesis or obstruction of the lower genital tract (7), and rupture of an ovarian cyst in a newborn infant (22).

The method of formation of ascites in cases of urethral obstruction is not very clear and has been the subject of much speculation. Where perforation of the bladder is found (10, 14), the explanation is evident, although the perforation may have been sealed off before birth. Case III falls into this category. Where no perforation is present, the pathogenesis of massive ascites remains obscure. Lord theorized that it might result from transudation through the walls of the dilated urinary tract. In cases of leakage, even though the original fluid may have been fetal urine, equilibration with the extracellular fluid would occur so rapidly that the composition of the ascitic fluid would approach that of extracellular fluid (16). This is supported by the laboratory findings in Case III, in which the serum urea nitrogen, chlorides, sodium, and potassium closely approximate the levels in the ascitic fluid.

Since the fatalities in these very young subjects are due to rapidly supervening kidney damage, and since secondary dilatation of the urinary tract can progress rapidly postpartum, it is imperative that urethral obstruction be recognized and

appropriate therapy be instituted promptly (11).

(d) *Miscellaneous Causes of Fetal Ascites:* Syphilis no longer is considered a significant cause of neonatal ascites. Although cases of syphilitic cirrhosis have been described (9), congenital syphilis rarely leads to cirrhosis in the newborn (3). Peritonitis accompanying congenital syphilis has been mentioned as a rare cause of ascites (16), but no convincing reports are available. This also applies to hepatic gummata obstructing the portal venous system.

Chylous ascites is a very rare form of congenital ascites caused by obstruction of the thoracic duct (2, 15, 25).

ROENTGENOGRAPHIC FEATURES

Roentgenograms of the abdomen during the first hour of life will show similar findings in the presence of massive ascites regardless of the etiology. There is diffuse, homogeneous opacification of the abdomen, with bulging flanks and lack of peritoneal fat lines. In cases where perforation of the distal small bowel is present there will, of course, be no free air demonstrable in the peritoneal cavity on roentgenograms obtained within the first few hours after birth, because transit of gas through the stomach and bowel is delayed. Where there is no obstruction, although distal progress of the gas in the bowel is delayed, the bowel will not appear distended. This is demonstrated in Case III (Fig. 3), in which, at twenty-six hours, the bowel gas was still at the level of about mid-ileum. In all probability this is the result of disturbed bowel motility

and adynamic ileus secondary to the peritoneal fluid present.

When bladder neck obstruction is present, the cysto-urethrogram is diagnostic, indicating obstruction at or below the vesical neck; Case III (Fig. 4) is an example. Early in life, the valvular action of the urethrovesical junction is unimpaired; moreover, the hypertrophy of the bladder may act to compress the distal urethral orifice, and reflux into the ureters may not be seen on the cystogram.

CONCLUSION AND SUMMARY

Neonatal ascites not associated with generalized edema is a rare condition, which should be considered an emergency since the prognosis is exceedingly poor unless there is prompt correction of the usually underlying congenital anomaly.

The anomaly, in the large majority of cases, involves the gastrointestinal system, the porto-hepatic organs, or the genitourinary system. The probable site can usually be determined preoperatively by clinical means. Roentgenologically, the abdominal changes are nonspecific, but contrast examination of the lower genitourinary tract may be diagnostic.

The literature is reviewed and 3 cases, one falling into each group of underlying anomalies, are added.

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REFERENCES

1. ABT, A. F.: Ascites in Infants. *M. Clin. North America* 16: 507-575, September 1932.
2. ABT, I. A.: Fetal Peritonitis. *M. Clin. North America* 15: 611-622, November 1931.
3. ANDERSON, W. A. D.: Pathology. St. Louis, C. V. Mosby Co., 2nd ed., 1953, p. 277.
4. BELLIN, L. B., AND BAILIT, I. W.: Congenital Cirrhosis of the Liver Associated with Infectious Hepatitis of Pregnancy. *J. Pediat.* 40: 60-63, January 1952.
5. BOIKAN, W. S.: Meconium Peritonitis from Spontaneous Perforation of the Ileum in Utero. *Arch. Path.* 9: 1164-1183, June 1930.
6. BIRNBAUM, R., AND BLACKER, G.: A Clinical Manual of the Malformations and Congenital Diseases of the Foetus. Philadelphia, P. Blakiston's Son & Co., 1912, p. 284.
7. DORLAND, W. A. N.: Watery Accumulations in Fetal Abdomen Obstructing Labor. *Am. J. Obst. & Gynec.* 79: 474-489, 1919.
8. FISCHER, A. E.: Fetal Peritonitis: Report of Case Following Spontaneous Rupture of Large Intestine. *Am. J. Dis. Child.* 36: 774-784, October 1928.
9. FORDYCE, W.: Intra-Uterine Ascites, Its Obstetrical Significance and Pathology. *Teratologia* 161: 143-157, 1894.
10. FRANCE, N. E., AND BACK, E. H.: Neonatal Ascites Associated with Urethral Obstruction. *Arch. Dis. Childhood* 29: 565-568, December 1954.
11. GROSS, R. E.: The Surgery of Infancy and Childhood. Its Principles and Techniques. Philadelphia, W. B. Saunders Co., 1953, pp. 163, 164, 508, 738.
12. HUNTER, R. H.: Foetal Ascites. *Lancet* 2: 999-1001, Nov. 5, 1932.
13. DAVIS, J. A. (for JAMES, U.): Congenital Urethral Obstruction Presenting as Ascites in the Neonatal Period. *Proc. Roy. Soc. Med.* 45: 401, June 1952.
14. KING, T. W.: Case of Disease in the Fetus: Impervious Urethra; Accumulated Urinary Secretion; Dilated Ureter; Bursting of the Distended Bladder; Peritonitis and Ascites at the Fourth Fetal Month. *Guy's Hosp. Rep.* 2: 508-518, 1837.
15. LAING, C. R., AND SCOTT, R. B.: Chylous Ascites. Report of a Case with Recovery and Survival After Fourteen Years. *J. Pediat.* 44: 191-194, January 1954.
16. LORD, J. M.: Foetal Ascites. *Arch. Dis. Childhood* 28: 398-403, October 1953.
17. MINKOWSKI, A., SAINTE-ANNE DARGASSIES, S., ARMAGANIDOU, D., BOURGONNIER, L., HEBERT-JOUAS, C., AND PELLERIN, D.: Ascite foetale avec hydramnios; évolution exceptionnelle vers la guérison; revue critique de la physiopathologie du liquide amniotique. *Études néo-natales* 6: 25-37, March 1957.
18. NELSON, W. E.: Textbook of Pediatrics. Philadelphia, W. B. Saunders Co., 6th ed., 1954, p. 715.
19. NEUHAUSER, E. B. D.: The Roentgen Diagnosis of Fetal Meconium Peritonitis. *Am. J. Roentgenol.* 51: 421-425, April 1944.
20. PARROTT, R. H.: Congenital Urethral Valve with Apparent Ascites. *Clin. Proc. Child. Hosp., Wash., D. C.* 7: 309-313, 1951.
21. PORAK: *Bull. de la Soc. Anat.*, 1875, p. 834.
22. TIETZ, K. G., AND DAVIS, J. B.: Ruptured Ovarian Cyst in a Newborn Infant. *J. Pediat.* 51: 564-565, November 1957.
23. PALTAUF, A.: Die spontanen Dickdarmpfortur des Neugeborenen. *Virchows Arch. f. path. Anat.* 111: 461-474, 1888.
24. SILVER, H. K., HUFFMAN, P. J., AND NAKASHIMA, I. I.: Fetal Ascites. *Am. J. Dis. Child.* 96: 268-271, September 1958.
25. WEGNER, E. S.: Congenital Chylous Ascites Apparently Cured by Ruotte's Operation (Venous Peritoneal Anastomosis). *Am. J. Dis. Child.* 47: 586-590, March 1934.
26. ZILLNER, E.: Rupture of Sigmoid Flexure Intra-Partum. *Virchows Arch. f. path. Anat.* 96: 307, 1884.

(Pro le summario in interlingua, vider le pagina sequente)

SUMMARIO IN INTERLINGUA

Massive Ascites Neonatal

Ascite neonatal, non associate con edema general, es un condition rar que debe esser considerate como un problema urgente, proque le prognose es malissime si le usualmente subjacente anormalitate congenite non es corrigite promptemente.

In le grande majoritate del casos, le anormalitate concerne le systema gastrointestinal, le organos porto-hepatic, o le systema genito-urinari. Usualmente le sito probabile pote esser determinate per medios clinic ante le operation. Roent-

genologicamente le alterationes abdominal es non-specific. Il occorre un diffuse e homogenee opacification del abdomine, con flancos extruse e le absentia del lineas properitoneal de grassia. In le presentia de un obstruction del cervice vesical, le cysto-urethrogramma es diagnostic, reflectente obstruction al cervice vesical o infra illo.

Es presentate un revista del litteratura. Tres casos, un in cata un del gruppos de anormalitates subjacente, es addite.



The Roentgen Findings in *Pneumocystis Carinii* Pneumonia¹

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RESPIRATORY DISORDERS remain the major cause of infant morbidity and even mortality in spite of many new fields of interest and research by pediatric, surgical, and roentgen investigators. The discouragingly high incidence of death in this category is obviously related to the anatomic state of the lungs and the overall stage of development of the patients. Premature infants, for example, have a high incidence of hyaline membrane disease which does not respond well to treatment and accounts for thousands of deaths each year (8). Also, new entities are becoming apparent—actually new diseases or conditions heretofore unrecognized and included in old nondescript categories. This report will deal with one of the second group.

Pneumocystis carinii pneumonia, or interstitial plasma-cell pneumonia, cannot accurately be described as new, since several hundred cases have been reported from Europe as well as some from America (5, 7, 10, 11, 13, 15, 19-22). American reports, however, have been limited to relatively recent identification of isolated cases (10, 15, 17, 18, 20). Much has been written abroad and to a lesser extent in the United States about the etiology, the endemic nature, and other aspects of the disease, but the characteristic roentgen findings have received little attention.

The purpose of this paper is twofold. One is to remind the radiologist that this is a clinical problem not as rare as formerly believed. The second is to describe what one of the authors (S. B. F.) feels is a characteristic roentgen diagnostic picture that should facilitate antemortem diagnosis, and lead to effective therapy.

CLINICAL FINDINGS

The clinical diagnosis of *Pneumocystis carinii* pneumonia is nonspecific and is

reached only after a process of deduction. The development of an antigen for skin testing does offer hope for a positive diagnosis without resorting to lung biopsy (5). The disease usually attacks the premature or feeble full-term infant during the second to fifth month of life. The onset in most instances is insidious, with a relative absence of symptoms or persistent mild upper respiratory infections. Diarrhea often precedes the full-blown clinical picture. The following findings have been reported as common, even though they are nonspecific in themselves: restlessness, anorexia, dyspnea without fever, tachypnea, cough, increased respiratory rate, cyanosis, and sternal retraction (7, 10, 11, 13-15, 18, 19).

The point which cannot be overemphasized is the discrepancy between severe dyspnea and the lack of physical findings. This is probably the single most important clue to the clinical diagnosis. Respiration becomes abdominal, the cough is unproductive, and cyanosis increases in spite of oxygen therapy. Emphysema with a few scattered râles may be the only physical finding. The hemogram is not characteristic. Mortality has been reported to vary from 15 to 100 per cent (10, 15).

ETIOLOGY

It is obvious that the roentgenologist and, to a lesser extent, the pathologist are not in the position of an epidemiologist in discussing the etiology of *Pneumocystis carinii* pneumonitis. Suffice it to say that qualified observers (5, 10, 11, 15) believe that the parasite *Pneumocystis carinii*, found in South America, Europe, and now in the United States, is the etiologic agent. It is discovered in lung biopsy material and in autopsy specimens from patients who have died from so-called

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interstitial plasma-cell pneumonia. For a discussion of the protozoan or fungous nature of the process the reader is referred to Gajdusek's article (10). The organism is rarely found in children or adults with chronic infections or cancer, but it has been identified somewhat more frequently in association with cytomegalic inclusion disease (10, 14, 20-22). In spite of this, we do not join the group which feels that the two conditions represent a single entity.

The cases of atypical virus pneumonia reported by Adams (1-4) from the University of Minnesota Hospitals have been included in the same category as *Pneumocystis carinii* pneumonia by some writers, but neither Adams nor the present authors are in agreement with this view.

PATHOLOGY

On gross examination, the lungs of patients who have died of *Pneumocystis carinii* pneumonia are extremely heavy, voluminous, and almost uniformly abnormal, due to lack of aeration, the appearance corresponding with the roentgen picture to be described later. The contours of the lung, both *in situ* and after removal from the thoracic cavity, remain constant. Because of the absence of air, no crepitation can be elicited on palpation. The specimens are firm and rubbery. No suppuration or caseation is present. The pleural spaces are free of fluid and fibrin. The tracheobronchial lymph nodes are not abnormal. The major branches of the tracheobronchial tree, the pulmonary vessels, the heart, and the great vessels are normal (6, 10).

Hematoxylin and eosin stains of the lung show uniform and extensive changes. The interstitial tissues are infiltrated by mononuclear cells. There are few or no polymorphonuclears. The involved interstitial tissue compresses and collapses the alveolar spaces and ducts. A few of the latter are dilated and this accounts for the "halo" emphysema (see below), exclusive of some reported peripheral emphysema. The Central European reports describe

the plasma cell as predominant, whereas British, Canadian, and United States observers have found it to be scarce or absent. In the group of *Pneumocystis carinii* pneumonitis complicating gammaglobulin deficiencies due to gammaglobulin synthesis failures, the plasma cells are characteristically absent (6). Pleural and bronchial epithelium are normal. No intracellular inclusion bodies are found. The abundant, honeycombed exudate, almost filling the small air spaces and present in smaller amounts in major branches of the bronchial tree, is quite characteristic in sections stained with hematoxylin and eosin. Large septal cells lining the alveoli can be seen in most cases, and alveolar capillaries seem devoid of blood in some sections (6, 10).

Hematoxylin and eosin stains do not show the parasites. They are demonstrated by Giemsa, Masson, silver impregnation, and Schiff stains, within the vacuoles of the honeycombed exudate. They are irregular, take a nuclear stain, and are embedded in a mucoid envelope (10).

ROENTGEN FINDINGS

The roentgen manifestations of *Pneumocystis carinii* pneumonitis have been largely disregarded. It has been said to present a "ground-glass" appearance, a relatively worthless term to the radiologists (9, 15). Jacob (12) described specific findings. The characteristic features in our limited material as well as in the illustrations in the literature reviewed are impressive.

The initial picture may not be too diagnostic. An infiltrate originating at the hilus and extending peripherally may at first glance resemble edema (Fig. 1), without the clinical findings of that condition. On closer observation, even in the early stage, a generalized granular pattern can be distinguished. The evolution of the granular picture without the antecedent infiltrate stage is very significant (Fig. 3). Associated with the coalescent, nodular pattern a loculated or "halo" emphysema

surrounding the non-aerated patches or some peripheral general emphysema (Fig. 1) may be seen. This corresponds to the pathologic finding of isolated, dilated alveoli and alveolar ducts which might encompass patches of non-aerated lung (10). The most characteristic picture, which also corresponds completely with the pathologic findings, is the finely granular peripheral pattern distributed throughout both lung fields (Figs. 2 and 4), not unlike the peripheral atelectasis seen in hyaline membrane disease (8). The factor common to the two entities from a roentgen standpoint is the absence of aeration peripherally, not a similarity of the underlying pathologic process. Thus the most striking roentgen picture is a peripheral granular appearance progressing through coalescent nodular and/or coalescent patchy "atelectasis" with emphysema, to complete peripheral "atelectasis." An important associated observation, which is probably significant, is the absence of hilar adenopathy. This was true not only of our cases, in which agammaglobulinemia was present, but also of cases in the literature in which this did not occur. The absence of lymphoid tissue changes in chronic infections associated with agammaglobulinemia has been radiographically described (16).

The peripheral atelectasis mentioned above is easily differentiated from pneumonic infiltrates. If *Pneumocystis* occurred in the newborn period, it could not be easily differentiated from peripheral alveolar atelectasis of hyaline membrane disease. Clinical history and age, as well as correlation with thoracic cage development beyond the newborn stage, help to exclude the latter condition.

During the active stage of progressive interstitial pneumonia which is evolving into a chronic fibrosing process (Hamman-Rich syndrome), the patchy and granular infiltrate (Fig. 5), with or without loculated emphysema, might be confused with *Pneumocystis*, but the end-result of sparse fibrosis in nonfatal cases is not likely to cause confusion (Fig. 6).

Radiographically, fibrocystic disease might be considered, simply because of the history of a chronically ill infant who fails to thrive, etc. Age, chronic bronchopneumonia, familial history, laboratory findings, and characteristic radiographs clearly differentiate the diseases.

CASE REPORTS

CASE I: D. O. was first seen at the University of Minnesota Hospitals at the age of one year, when he was chronically ill and debilitated. He had been hospitalized elsewhere at the age of six months and thereafter his hospital confinement was almost continuous. The admission diagnosis at the University of Minnesota Hospitals was probable fibrocystic disease, but sweat tests, etc., had been negative. A previous work-up did show a pancytopenia and a slightly depressed hemoglobin. The gamma globulin was 0.34 gm. per 100 c.c.

The child was wasted, the chest wall was retracted, and a few scattered râles were elicited. The liver was palpable 3 cm. below the costal margin. The sweat test was normal. The albumin was 1.9 gm. per 100 c.c., globulin 2.1 gm. per 100 c.c. The electrophoretic pattern showed 0.1 gm. gamma globulin per 100 ml. of blood. The blood indices and all skin tests were normal. Cultures and lung biopsies were negative for plasma cells.

Roentgen studies showed patchy, "edema-like" infiltrates actually composed of conglomerate granules and nodules with surrounding loculated, "halo" emphysema (Fig. 1). These became more coalescent and finally resulted in complete non-aeration of the peripheral lung fields (Fig. 2).

In differential diagnosis agammaglobulinemia, plasma-cell pneumonia, fibrocystic disease, histoplasmosis, and hemosiderosis were considered.

Pathologically the gross and histologic findings were primarily those described under the general heading of "Pathology" in the body of this report. The silver stain showed the multinucleated organisms of *Pneumocystis carinii*.

CASE II: D. N. was transferred to the University of Minnesota Hospitals at one month of age after having had an ileostomy and partial colectomy elsewhere because of extensive aganglionosis discovered on the sixth day of life.

On admission, the infant was debilitated, with no findings referable to the chest. Electrolyte balance was restored and he was discharged but was readmitted four months later because of growth failure as well as debilitation. In spite of supportive therapy, he continued to deteriorate. Respiratory distress with grunting respirations and cyanosis developed, but the child was afebrile. The lungs were clear to percussion and auscultation. The only positive laboratory findings were a markedly de-

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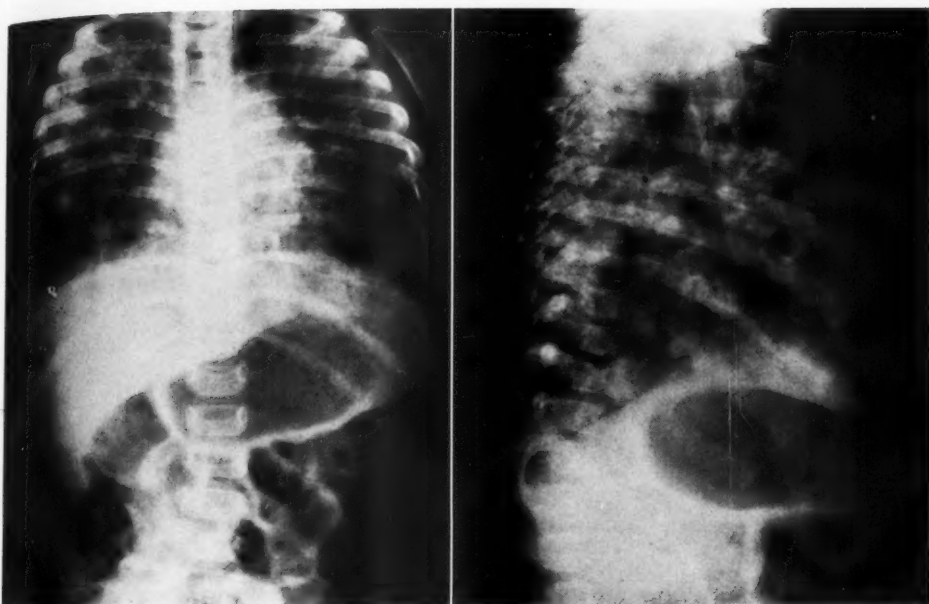


Fig. 1. Case I. Frontal and lateral projections of chest showing diffuse involvement of both lung fields. The original films show diffuse granularity which coalesced in widespread areas. Some of these zones show loculated or "halo" emphysema exclusive of peripheral diffuse emphysema of both lower lobes. Bronchi are silhouetted by air.

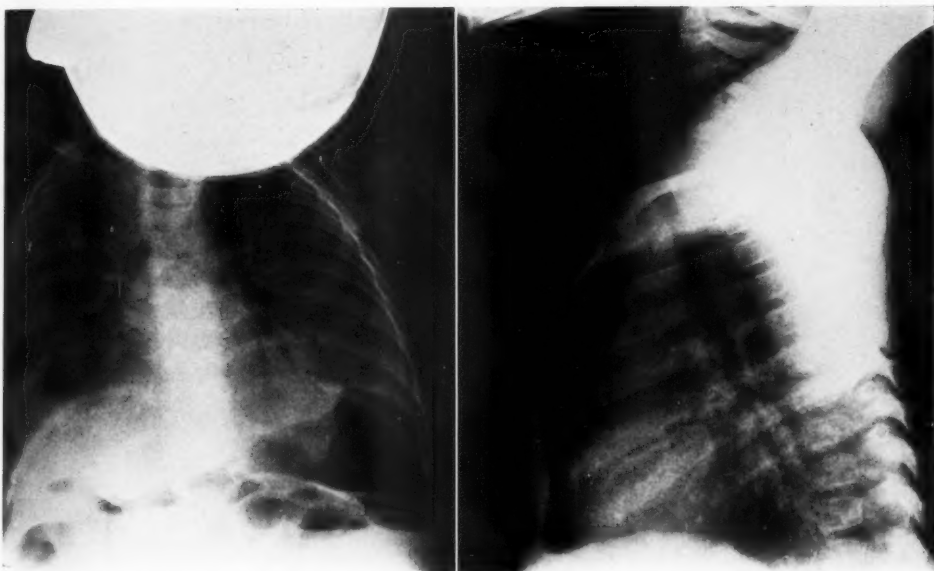


Fig. 2. Case I. Terminal frontal and lateral projections showing almost complete lack of aeration of the peripheral lung fields, with coalescent granularity. Air-filled bronchi stand out in relatively bold relief. No adenopathy is seen.

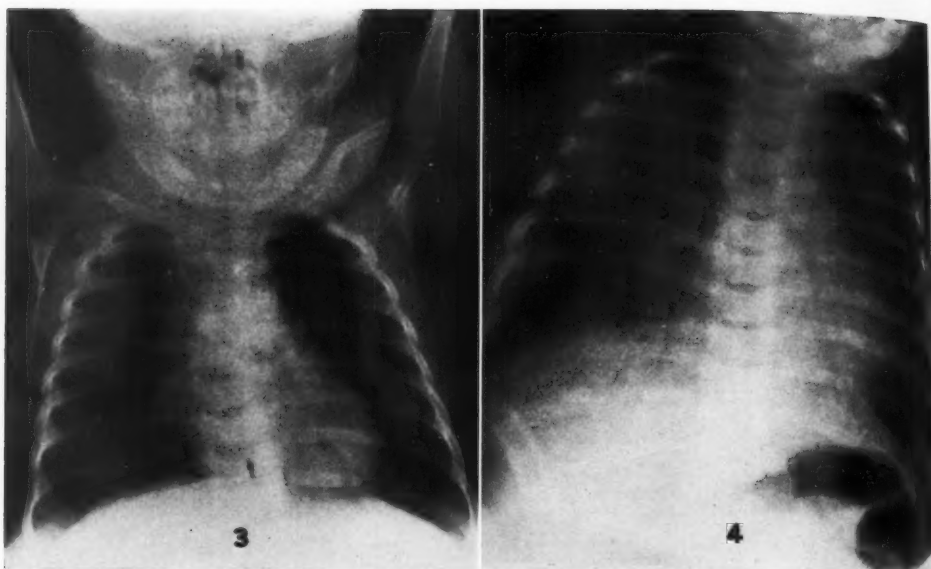


Fig. 3. Case II. Frontal projection at time of admission, showing only hyperaeration of both lung fields.
 Fig. 4. Case II. Radiograph taken shortly before death showing complete peripheral absence of aeration with resultant blurring of cardiac margins, suggesting *Pneumocystis carinii* pneumonia. Air-filled bronchi stand out by contrast even on technically poor bedside examination. No adenopathy is apparent.

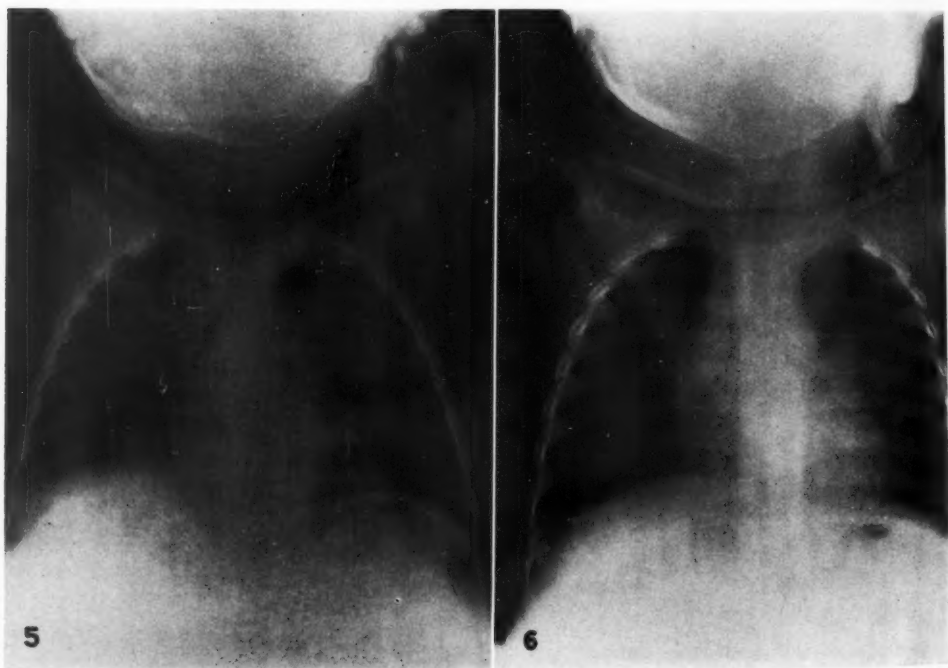


Fig. 5. Residual consolidation in right upper lobe two months after acute pneumonia with some bilateral nodularity in perihilar areas. To be differentiated from *Pneumocystis* pneumonia.
 Fig. 6. Final persistent radiographic picture six months after acute interstitial pneumonia which has now cleared. Interstitial fibrosis persists. The patient is clinically well.

pressed gamma globulin level and a relative eosinophilia (11-25 per cent). The initial radiograph of the chest showed nonspecific hyperaeration (Fig. 3). In rapid sequence during a one-week period the picture progressed from an early reticulogranularity to a granulonodular pattern, and finally to a complete peripheral "atelectasis" suggesting *Pneumocystis* (Fig. 4).

The infant died one and one half months after his second hospitalization. Autopsy findings were similar to those described in the body of the report under "Pathology." The organisms were found by silver staining.

SUMMARY

The clinical, etiologic, and pathologic findings of *Pneumocystis carinii* pneumonitis are briefly reviewed and discussed.

Roentgen findings which may suggest the diagnosis, without a lung biopsy, are a generalized granular pulmonary parenchymal pattern which can progress immediately to coalescing nodules, and finally to a complete peripheral absence of aeration. The early granularity may progress less directly to patches of coalescence with surrounding loculated emphysema simulating "edema," followed by further coalescence with peripheral general emphysema, and finally complete peripheral non-aeration.

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REFERENCES

- ADAMS, J. M.: Preliminary Report: New Form of Virus Pneumonitis Occurring Epidemically Among Newborn Infants. *Proc. Soc. Exper. Biol. & Med.* **46**: 114-116, January 1941.
- ADAMS, J. M.: Primary Virus Pneumonitis with Cytoplasmic Inclusion Bodies; Study of an Epidemic Involving 32 Infants with 9 Deaths. *J.A.M.A.* **116**: 925-933, March 8, 1941.
- ADAMS, J. M., GREEN, R. G., EVANS, C. A., AND BEACH, N.: Primary Virus Pneumonitis; Comparative Study of 2 Epidemics. *J. Pediat.* **20**: 405-420, April 1942.
- ADAMS, J. M.: Personal communication.
- BARTA, K., DVORACEK, C., AND KADLEC, A.: Komplementbindungs-Reaktion bei Pneumozysten-Pneumonien. *Schweiz. Ztschr. f. allg. Path. u. Bakt.* **18**: 22-32, 1955.
- BURKE, B. A., KROVETZ, L. J., AND GOOD, R. A.: Occurrence of *Pneumocystis Carinii* Pneumonia in Children with Agammaglobulinemia. In press.
- DEAMER, W. C., AND ZOLLINGER, H. U.: Interstitial "Plasma Cell" Pneumonia of Premature and Young Infants. *Pediatrics* **12**: 11-22, July 1953.
- FEINBERG, S. B., AND GOLDBERG, M. E.: Hyaline Membrane Disease: Preclinical Roentgen Diagnosis. A Planned Study. *Radiology* **68**: 185-191, February 1957.
- GARSCHKE, R.: Zur klinischen Bedeutung der Röntgendiagnostik bei der interstitiellen Pneumonie frühgeborener Kinder. *Fortschr. a. d. Geb. d. Röntgenstrahlen* **75**: 125-138, August 1951.
- GAJDUSEK, D. C.: *Pneumocystis Carinii*; Etiologic Agent of Interstitial Plasma Cell Pneumonia of Premature and Young Infants. *Pediatrics* **19**: 543-565, April 1957.
- GRUENWALD, P., AND JACOBI, M.: Mononuclear Pneumonia in Sudden Death or Rapidly Fatal Illness in Infants. *J. Pediat.* **39**: 650-662, December 1951.
- JACOB, G.: Gibt es ein typisches Röntgenbild der klinisch eben manifesten interstitiellen Pneumonie der Frühgeburten? *Fortschr. a. d. Geb. d. Röntgenstrahlen* **80**: 697-708, June 1954.
- KIDDER, L. A.: Cerebral and Visceral Inclusion Disease of Infancy. *Am. J. Clin. Path.* **22**: 870-878, September 1952.
- KODOUSEK, R.: Nachweis der Hale-positiven Polysaccharide in den Zellen der Inklusionszytomegalie und Anwendung der Hale'schen Methode zur histologischen Diagnostik dieser Erkrankung. *Schweiz. Ztschr. f. allg. Path. u. Bakt.* **17**: 641-648, 1954.
- LUNSETH, J. H., KIRMSE, T. W., PREZYNA, A. P., AND GERTH, R. E.: Interstitial Plasma Cell Pneumonia. *J. Pediat.* **46**: 137-145, February 1955.
- MARGULIS, A. R., FEINBERG, S. B., LESTER, R. G., AND GOOD, R. A.: Roentgen Manifestations of Congenital Agammaglobulinemia. *Radiology* **69**: 354-359, September 1957.
- ROWE, C. W.: *Pneumocystis Carinii* Pneumonia. *Radiology* **75**: 257-261, August 1960.
- STERNBERG, S. D., AND ROSENTHAL, J. H.: Interstitial Plasma Cell Pneumonia. *J. Pediat.* **46**: 380-393, April 1955.
- VANEK, J., JIROVEC, O., AND LUKES, J.: Interstitial Plasma Cell Pneumonia in Infants. *Ann. paediat.* **180**: 1-21, January 1953.
- WELLER, R. W.: Giant Cell Pneumonia with Inclusions. *Pediatrics* **10**: 681-685, December 1952.
- WYATT, J. P., HEMSATH, F. A., AND SOASH, M. D.: Disseminated Cytomegalic Inclusion Disease in an Adult with Primary Refractory Anemia and Transfusional Siderosis; Report of a Case. *Am. J. Clin. Path.* **21**: 50-55, January 1951.
- WYATT, J. P., SIMON, T., TRUMBULL, M. L., AND EVANS, M.: Cytomegalic Inclusion Pneumonitis in the Adult. *Am. J. Clin. Path.* **23**: 353-362, April 1953.

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SUMMARIO IN INTERLINGUA

Le Constataciones Roentgenologic in Pneumonia a Pneumocystis carinii

Es revistate e discutite brevemente le constataciones clinic, etiologic, e pathologic de pneumonitis a *Pneumocystis carinii*. Un puncto que non pote esser signalate troppo emphaticamente es le discrepantia inter le presentia de un sever dyspnea a le manco de constataciones physic. Le reportos pathologic signala que le pulmones de pacientes morte per iste condition es extremamente pesante, voluminose, e quasi uniformemente anormal in consequentia del defective aeration. Isto se trova in congruentia con le observationes roentgenographic.

Le constataciones roentgenographic que

pote suggerer iste morbo es sublineate in le interesse del effectuation de un diagnose ante morte sin le uso de biopsia pulmonar. Ille constataciones es un generalisate configuration granular del parenchyma pulmonar con le possibilitate de un progresso immediate ad un stadio de nodulos coalescente e finalmente ad le complete absentia peripheric de aeration. Le precoce granularitate pote etiam progredier minus directemente al formation de maculas de coalescentia con circumjacente emphysema loculate que simula "edema," sequite per plus coalescentia con peripheric emphysema general e finalmente per un complete non-aeration peripheric.



Pulmonary Metastasis from Trophoblastic Tumors¹

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TROPHOBLASTIC tumors frequently metastasize to the lungs. When, in the presence of known trophoblastic disease of the pelvis, the chest film reveals one or more pulmonary nodules, the radiologist usually diagnoses metastatic choriocarcinoma. Not infrequently this interpretation is wrong. Recent literature points out that hydatidiform moles and their variants occasionally metastasize to the lungs and that these benign metastases will regress spontaneously or following x-ray therapy.

The appearance, growth, and regression of trophoblastic lesions, regardless of their location within the body, are reflected by changing titers of chorionic gonadotropin in the blood serum and urine. As viable trophoblastic cells proliferate, the gonadotropin level rises; with involution the level drops to zero unless another focus of trophoblastic activity occurs. The stimulus for growth and involution are unknown.

It is beyond the scope of this report to discuss the microscopic and clinical variants of trophoblastic tumors. Suffice it to state that they range from the benign hydatidiform mole with its typical trophoblastic villi to the frankly malignant choriocarcinoma, and that there is an intervening group of tumors known as chorioadenoma destruens which are considered benign but exhibit many microscopic features of malignancy. Often the clinical course and outcome determine the benign or malignant nature of a tumor.

Hunt *et al.* (1) reported 2 cases of chorioadenoma destruens with pulmonary metastases which regressed completely following roentgen therapy to the chest. Both of these patients were alive and well, clinically free of disease, twenty-five months later. In 1 there were a large pelvic mass, multiple pulmonary nodules,

and a high chorionic gonadotropin assay on the twenty-four-hour collection of urine. The other patient underwent hysterectomy for continued uterine bleeding eight weeks after passing a hydatidiform mole. Thirteen days later a solitary pulmonary nodule appeared, and the urinary chorionic gonadotropin level was elevated. One week after conclusion of roentgen therapy to the chest, the urinary assay for chorionic gonadotropin was negative. Five months later the pulmonary nodule had disappeared. The histologic diagnosis in both cases was chorioadenoma destruens, a benign lesion. If further evidence of malignancy should appear, the diagnosis of choriocarcinoma, according to Hunt *et al.*, would be unequivocal. On the other hand, if both patients continue to be well, it must be assumed either that the irradiation effected a cure of choriocarcinoma or, more likely, that the pulmonary lesions were benign metastases of chorionic elements from an invasive mole.

Novak and Seah (2) in their discussion of choriocarcinoma cite 3 cases of chorioadenoma destruens with pulmonary metastasis. In 1 patient, the lesion was diagnosed from curettings as a benign mole, but after examination of the uterus the classification was changed to chorioadenoma destruens. This patient later died, without autopsy. The other 2 patients were alive and well for four and eight years, respectively. Pulmonary lesions regressed spontaneously in 1 and after chest irradiation in the other.

Delfs (3) had a patient who passed a large, benign mole of five to six months duration. Eighty-one days later a partial right upper lobectomy for a single pulmonary nodule was performed. Microscopic examination revealed a molar metastasis with well defined villi which

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Fig. 1. Pelvic mass of four and a half to five months gestation, with no fetal parts visible.

appeared cytologically benign. Subsequently paralysis of the lower extremities developed, which at laminectomy was found to be due to an extradural molar metastasis.

Logan and Motyloff (4) described 3 cases with pulmonary metastasis, high gonadotropin titers, and negative findings on curettage after each patient had initially passed benign, chorionic tissue. One patient had a complete hysterectomy with bilateral salpingo-oophorectomy, following which she received x-ray therapy to the pelvis and chest. Positive titers of chorionic hormone and positive pulmonary roentgen findings persisted for two years. A final diagnosis of choriocarcinoma was made, based on the microscopic study of the uterus. The fact that this patient was well and free of disease seven years later challenges this diagnosis. One wonders whether this is another example of benign invasive mole with pulmonary metastasis.

Logan and Motyloff's second patient was a woman who had multiple pulmonary nodules which regressed spontaneously in five weeks. Concurrently the gonadotropin titer dropped to normal, and she has remained asymptomatic. The third case was similar except that the patient underwent hysterectomy, following which the pulmonary lesions regressed spontaneously.

The following case, presented elsewhere (5) in more detail, illustrates many of the common clinical and radiological problems associated with trophoblastic tumors.

A 22-year-old primigravida, first seen two months following her last menstrual period, exhibited early signs of pregnancy. The uterus was of the size to be expected at five to six weeks. In the next two and a half weeks it grew more rapidly than anticipated and reached a level of 1.0 cm. below the umbilicus—nearly four months size. Quantitative pregnancy tests were highly positive. X-ray examination of the abdomen revealed a pelvic mass of four and a half to five month gestation, with no fetal parts visible (Fig. 1). Under observation for four days in the hospital, the uterus reached a level of 2.0 cm. above the umbilicus. An abdominal hysterotomy was performed and a hydatid mole removed from the uterine cavity.

Roentgenograms of the chest two days postoperatively, initially interpreted as normal, showed in retrospect a 3-mm. nodular density in the left upper lobe (Fig. 2). Seven days postoperatively the patient had a sudden, severe hemorrhage from the uterus controlled by intravenous therapy and blood replacement. Five weeks later an Aschheim-Zondek test became positive and along with persistent minimal bleeding led to the suspicion of an invasive mole or choriocarcinoma. Dilatation and curettage revealed only decidua tissue. In spite of the normal curettage, the pregnancy test remained positive. Repeat chest roentgenogram, ten weeks following the previous one, revealed three nodular shadows in the left upper lobe, the largest of which measured 2 cm. in diameter (Fig. 3). These were interpreted as metastatic foci, most likely from choriocarcinoma. Curettage at this time still showed only decidua tissue.

The patient was next seen at the Mayo Clinic, where for the first time in three months the twenty-four-hour urine specimen was entirely negative for chorionic gonadotropin. Because of the unchanging appearance of the chest roentgenogram and the possibility of a primary tumor or granuloma of the lung, in spite of the negative gonadotropin titer, a segmental resection of the anterior segment of the left upper lobe and superior segment of the left lower lobe was performed. Microscopic studies re-



Fig. 2. Postoperative roentgenogram of the chest, showing a small nodular density in the left upper lobe.

Fig. 3. Roentgenogram obtained ten weeks later, showing multiple nodular densities in the left upper lobe and an increase in size of the original nodule.

vealed infarcted decidual and probably placental villous tissue with secondary regional pneumonitis (Fig. 4). Postoperatively the patient has remained well, clinically free of disease, for four and a half years.

From the above case report and those cited from the literature, we can reach the following conclusions: Trophoblastic tumors are often difficult to classify. Their relative rarity gives the pathologist or gynecologist little opportunity to familiarize himself with their variable manifestations. Frequently certain types of hydatidiform moles and non-neoplastic lesions such as endometritis are wrongly diagnosed as choriocarcinoma; rarely is the latter misdiagnosed as benign. The interpretation of curettings is often inaccurate or misleading, since endometrial tissue may be sparse or fragmentary, or the trophoblastic lesions may be embedded

within the myometrium or be growing parametrically. Even after examination of the entire uterus, the diagnosis can remain in doubt, since the microscopic features of anaplasia and invasiveness are unreliable indices of relative malignancy.

The microscopic features of choriocarcinoma are clear-cut and unmistakable, while those of the invasive, benign mole may be indecisive in terms of malignancy or benignancy and require the astute judgment of an experienced observer for correct interpretation. Nevertheless, the diagnosis of choriocarcinoma imparts a grave prognosis, while a diagnosis of an invasive or non-invasive mole favors a good outcome.

All forms of trophoblastic tumors metastasize. The presence, therefore, of a pulmonary lesion following passage or surgical removal of a benign mole is not

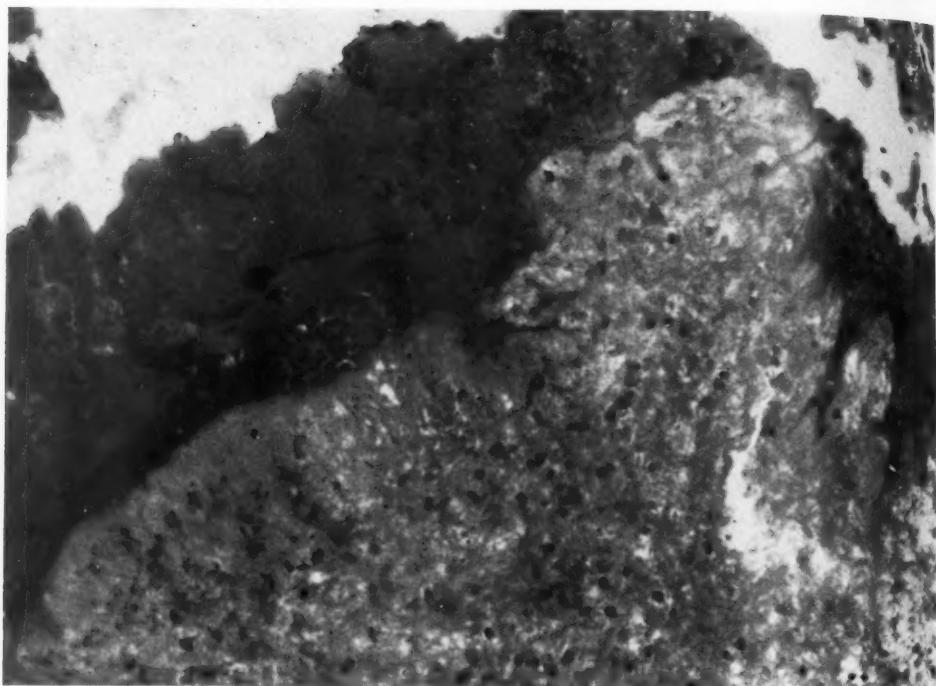


Fig. 4. Irregularly outlined villus with central necrosis and marginal distribution of trophoblast-like cells, all surrounded by necrotic material and hemorrhage.

indisputable evidence of malignancy. Pulmonary lesions which regress and then recur or continue to grow and increase in size and number, particularly where the chorionic gonadotropin remains elevated, are undoubtedly malignant. Those lesions which regress spontaneously and probably those lesions which regress following x-ray therapy, without recurrence, are most likely benign. Many of the cases reported in the literature as permanent remissions of choriocarcinoma are undoubtedly misdiagnosed forms of benign, invasive mole or chorioadenoma destruens. There are no characteristic roentgen features which distinguish between benign and malignant pulmonary metastases from trophoblastic tumors. Whether one chooses to call benign pulmonary lesions metastases, emboli, or "benign deportation of trophoblastic tissue" (terms used in gynecological literature) is of academic importance only.

The chorionic gonadotropin titer is the

best indication of trophoblastic activity. Rising titers indicate growth; falling titers indicate regression. Usually roentgen evidence of regression lags several months behind hormonal evidence of regression. In fact, the pulmonary lesion may enlarge initially in spite of falling or negative gonadotropin titers, due to a decidual reaction, similar to that occurring in the uterus, and secondary regional pneumonitis. The microscopic picture is predominantly one of necrosis, hemorrhage, and granulation reaction surrounding infarcted, decidual, and villous tissue. Thus the size of the lesion on x-ray examination is no indication of activity and growth unless serial studies depict progressive changes and gonadotropin titers confirm activity.

SUMMARY

1. All trophoblastic tumors metastasize. Benign pulmonary metastasis from in-

vative or non-invasive moles may occur in the absence of identifiable molar tissue elsewhere in the body.

2. There are no roentgen features which distinguish the benign from the malignant metastasis.

3. The best indication of a benign pulmonary lesion is a persistently falling or negative gonadotropin titer followed by complete roentgen regression of the tumor. Only in retrospect can a positive diagnosis of benign metastasis be made. Nevertheless, not all pulmonary nodules following passage of a benign mole should be labeled metastatic choriocarcinoma, since the latter diagnosis imparts a grave prognosis and may be erroneous.

4. We have reviewed several cases from the literature of benign pulmonary metastasis following passage of a mole and have added a case of our own. All the metastatic lesions regressed spontaneously or following x-ray therapy. Our case was unique in that there was

microscopic evidence of molar tissue in the resected specimen.

5. Recognition of this entity of benign pulmonary metastasis may help clarify some of the confusion that abounds as to the clinical course and management of trophoblastic tumors.

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REFERENCES

1. HUNT, W., DOCKERTY, M. B., AND RANDALL, L. M.: Hydatidiform Mole; Clinicopathologic Study Involving "Grading" as Measure of Possible Malignant Change. *Obst. & Gynec.* 1: 593-609, June 1953.
2. NOVAK, E., AND SEAH, C. S.: Choriocarcinoma of Uterus; Study of 74 Cases from Mathieu Memorial Chorionepithelioma Registry. *Am. J. Obst. & Gynec.* 67: 933-961, May 1954.
3. DELFS, E.: Quantitative Chorionic Gonadotrophin: Prognostic Value in Hydatidiform Mole and Chorionepithelioma. *Obst. & Gynec.* 9: 1-24, January 1957.
4. LOGAN, B. J., AND MOTYLOFF, L.: Hydatidiform Mole; A Clinical and Pathological Study of 72 Cases, with Reference to Their Malignant Tendencies. *Am. J. Obst. & Gynec.* 75: 1134-1148, May 1958.
5. JACOBSON, F. J., AND ENZER, N.: Hydatidiform Mole with "Benign" Metastasis to Lung. Histological Evidence of Regressing Lesion in Lung. *Am. J. Obst. & Gynec.* 78: 868-875, October 1959.

SUMMARIO IN INTERLINGUA

Metastase Pulmonar ab Tumores Trophoblastic

Es revistate plure casos de benigne metastase pulmonar post vacation de molas hydatidiforme super le base del reportos in le litteratura. Un nove caso es addite que illustra multes del commun problemas clinic e radiologic associate con tumores trophoblastic e lor metastases pulmonar. In iste caso evidentia microscopic de tissu molar esseva trovate in le resecate segmentos pulmonar.

Omne tumores trophoblastic es capace de metastase. Benigne metastases pulmonar ab invasive o non-invasive molas pote occurrer in le absentia de identificabile tissu molar in altere partes del corpore.

Le distinction inter benigne e maligne metastases non pote esser establite roentgenologicamente. Le melior indication de un benigne lesion pulmonar es un persistente declino o le negativitate del titro de gonadotropina sequite per le complete regression del tumor. Il es solmente in retrospecto que un diagnose positive de benigne metastase pote esser facite.

In despecto de iste incertitude, non omne nodulos pulmonar post le vacation de un mola deberea esser designate como metastatic choriocarcinoma, proque iste diagnose suggere un grave prognose e pote esser erronee.

Evaluation of Film Size in Cineradiography¹

JOHN A. CAMPBELL, M.D., EUGENE C. KLATTE, M.D., DONALD D. GRAY, R.T., and ALICE L. McCREA, M.S.

THE ADVENT of larger image-intensifying tubes with higher brightness gain has solved many of the problems of radiation dose and field size in cineradiography. Limited image detail remains as the most critical obstacle to be overcome if this method is to have a wider range of diagnostic usefulness.

It is the purpose of this presentation to evaluate the relative merits of film size alone as a determining factor in the quality of a cine-image. Obviously, the film can record an image no better in detail than the quality and adjustment of the image intensifier and lens system will produce. It is obvious, furthermore, that the larger of two films with the same emulsion characteristics will present a greater number of photosensitive grains to accept the image; hence it can potentially yield more detail. Because of the very limited resolving power of present-day image tubes, the question of whether there is any critical gain in diagnostic yield through the use of 35-mm. film is pertinent.

FACTORS AFFECTING THE EVALUATION OF FILM SIZE

In any attempt to evaluate a single factor in a cinefluorographic system, such as film size, it is important that the other factors affecting image resolution be controlled. Image tubes may range in resolving power from 25 to 50 line pairs per inch and there may be considerable variation in the resolution of tubes of the same manufacturer. Image-tube focus is quite critical and must be adjusted carefully during close observation of a reticle of wire mesh having a range of 20 to 40 line pairs per inch. Another factor affecting image-tube resolution is the scintillation effect. A certain number of information-bearing

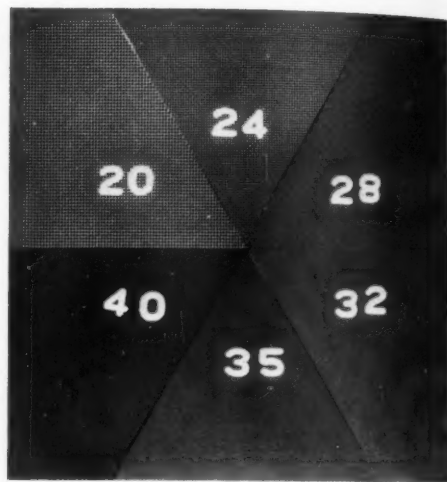


Fig. 1. Wire screen cloth test object. This direct radiograph shows the patterns of varying texture used for resolution tests on the cine-systems. The numerals indicate the number of line pairs per inch for each sector.

photons must be absorbed by the input phosphor of the image tube to form a clear image which may be amplified and then recorded. If the radiation input is small, due to a high gain image tube and fast lens system, the signal to noise ratio of the tube will be low, and an image of poor definition will be recorded. The lens system of available 16-mm. units is two to four times faster than of 35-mm. units, and it might be expected that scintillation would be more apparent in the faster system, with a resultant loss of image definition. In order to discount the scintillation effect on the comparison of 16-mm. and 35-mm. film size, the relative speed of the lens system was kept constant. This was done by stopping down the f 0.95 camera lens of the Picker unit to f 2.2 and the f 1.0 camera lens on the Philips unit to f 2.8. In this way, the same film

¹ From the Department of Radiology, Indiana University-School of Medicine, Indianapolis, Ind. This investigation was supported by the James Picker Foundation on recommendation of the Committee on Radiology, National Academy of Sciences-National Research Council. Presented at the Forty-sixth Annual Meeting of the Radiological Society of North America, Cincinnati, Ohio, Dec. 4-9, 1960.

density was obtained on both 16- and 35-mm. films with the same radiation dose. Because the Picker unit utilizes a synchronized pulsed exposure, the radiation dose rate was approximately half that of the Philips unit.

The resolving powers of lens systems vary, and this factor must be considered in the comparison of film size. Although a broad investigation of lenses was not carried out in this experiment, lens systems of the highest caliber available were used.

The lens system was focused by radiographing a reticle at multiple camera lens settings. The lens was then adjusted to that setting at which the best image definition was obtained.

A radiographic tube with a 1-mm. focal spot was utilized. The target-to-input phosphor distance was kept constant at 36 inches. Although a slight improvement in image resolution might have been obtained by using a 0.3-mm. focal spot, this would not affect the comparative resolution of 16-mm. and 35-mm. film.

METHOD OF EVALUATION

In general, image quality is judged by its resolution and its sharpness of detail, or "acutance." Resolution, or the ability to distinguish repetitive detail, is usually measured by test objects constructed of sets of bars or lines having indicated spatial frequencies in lines per millimeter or inch. After the film is exposed and processed, the images are examined under magnification. The coarse bars which are distinguished individually are resolved, but the fine bars merge into one another. The greatest spatial frequency, or the narrowest bars and spaces that can be resolved, is said to be the resolving-power limit.

Various objects to test resolving power have been used in cineradiography. Weinberg (1), Hallock (2), Ball (3), and others have reported their findings with a wire-screen cloth² having a 25 per cent open

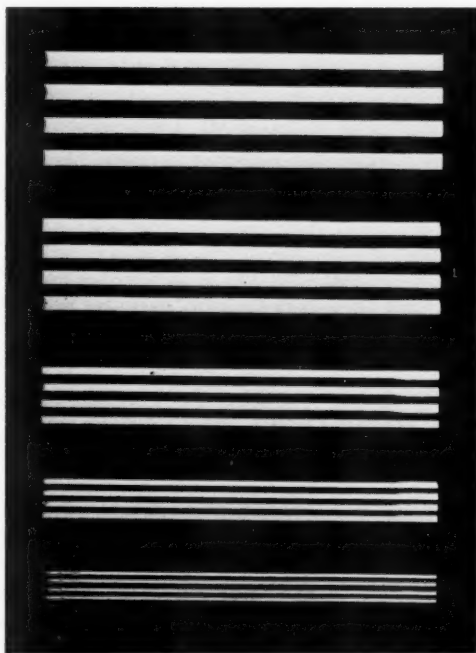


Fig. 2. General Electric lead reticle. The radiograph shows the different spatial frequencies which vary from 12 to 50 line pairs per inch.

area so that the lines and spaces are of equal width. By piecing several pie-shaped segments of wire cloth of different textures together, a test object can be made (Fig. 1) for measuring the resolution over the entire face of the image tube. The TV division of General Electric Co. (Milwaukee, Wis.) developed a flat plastic reticle constructed of parallel leaded bars with equal spaces between them. Such bars of varying width and depth were arranged in groups over the face of the plastic to give a useful range of spatial frequencies in lines per inch (Fig. 2).

Ter-Pogossian (4) has introduced another test object designed to study the effect of contrast on finite resolution. This consists of a plastic block in which cylindrical holes of similar graded diameters were filled with different dilutions of iodized contrast solutions (Fig. 3). With this, the density level at which linear objects of the same diameter are resolved may be determined.

²C. O. Jelliff Manufacturing Co., Southport, Conn.

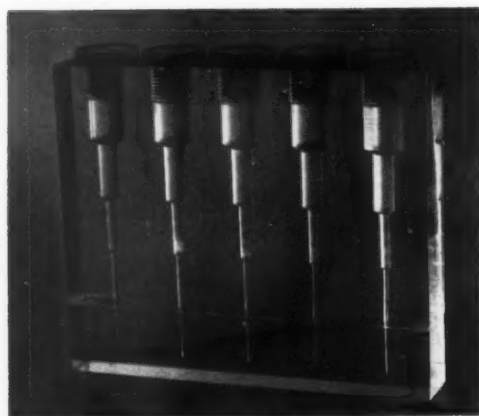


Fig. 3. Ter-Pogossian contrast test object. The cylindrical holes in the plastic block are identical in their varying calibers. These are filled with opaque contrast solutions of different dilutions to test their radiographic perceptibility.

pany (Eindhoven, The Netherlands) for studying the resolution of their electron image tubes. They used a brass plate 0.5 mm. thick into which was drilled a pattern of small holes of diameters varying from 0.2 to 0.7 mm., separated by spaces of equal width (Fig. 4).

Because none of these test objects allows an interpolation of the exact endpoint of resolution falling between two separate groups of line frequencies, and since no standard pattern for testing the resolution of image-amplifier tubes was commercially available, we developed our own test object for use in this study. The requirements set for this pattern were:

1. The lines and spaces should be of equal width.

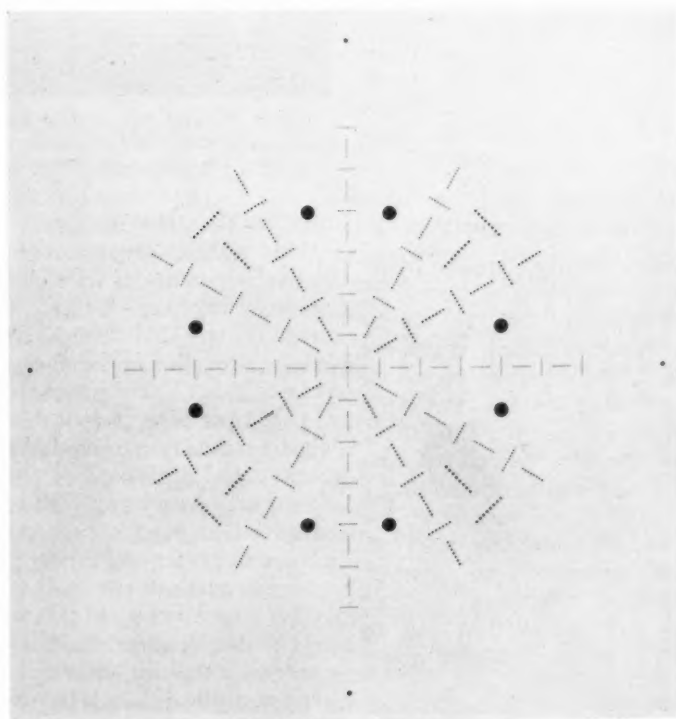


Fig. 4. Philips electric brass reticle. The roentgenogram shows the pattern of small holes of varying size. The holes and spaces are equal in width, and the rows running at 90° to one another are of the same caliber.

Still another test reticle was developed by the engineers of Philips Electric Com-

2. The depth of the lines should be the same throughout the pattern.

3. The gradation in line pairs per inch (one line pair being one line and one space) should be continuous to eliminate as much interpolation as possible.

4. The design should be such that all parts of the field from center to edge could be tested.

The final test object evolved was an 8-

per inch from a central point to the edge of the circle. The other four groups are centered at points outside the rim, radiating from it toward the center and decreasing continuously in line pairs per inch from the rim toward the center. This arrangement allows testing the edge of the field as well as the center.

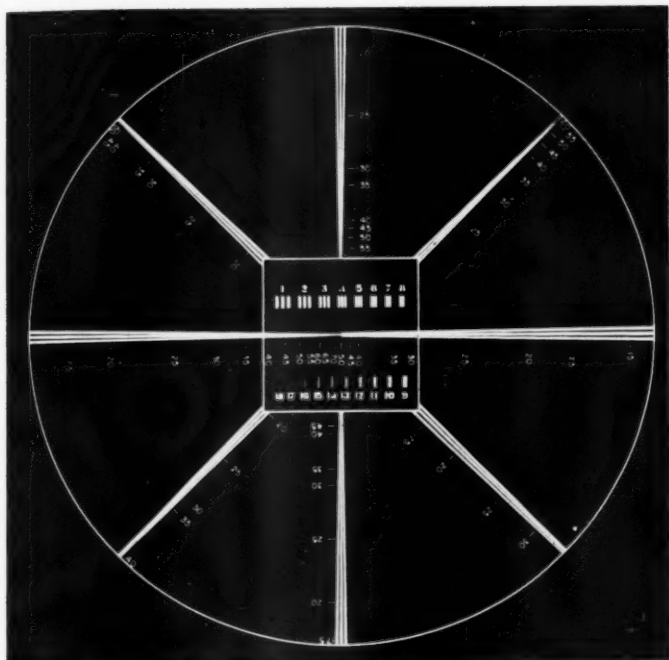


Fig. 5. Indiana University test pattern. The direct radiograph illustrates the pattern of the diverging and converging bars and spaces of varying lines per inch. Two convergent line groupings run into the center of the field. The small bar reticle measures the resolution on the areas of highest resolution of the image tube.

inch-diameter circle etched in plastic and filled with dental amalgam. Equal lines and spaces and continuous gradation in line pairs per inch were attained by using as lines and spaces equal sectors of a circle 0.36° each. There are eight groups of sectors, each group containing five sectors, making $2\frac{1}{2}$ line pairs per group. Each group of sectors is centered at a different distance from the rim of the circle to give the desired range of line pairs per inch. Four of the groups start from points inside the circle and radiate outward toward the rim, decreasing continuously in line pairs

Only two groups of sectors were brought to the center of the plate, since bringing all the groups to the center would lead to such a large number of lines in this small area that it would be difficult to distinguish between them. Instead, the central two-inch square area was converted into a line reticle.

The test pattern was drawn at three times natural size and reduced photographically to an 8-inch-diameter circle which was engraved on plastic by the Dupont "dycril" process. The lines were made opaque to x-rays by filling them

TABLE I: CAMERA AND LENS SPECIFICATIONS

Lens Characteristics	Philips 16-mm. Bell & Howell		Picker 16-mm. Kodak Cine Special		Philips 35-mm. Arriflex		Picker 35-mm. Photo Mechanisms	
	1st stage	2nd stage	1st stage	2nd stage	1st stage	2nd stage	1st stage	2nd stage
f. No.	1.5	1.0	1.0	0.95	1.5	2.0	1.0	1.4
Focal length (mm.)	100	25	50	25	100	75	50	58
Aperture	Open	2.2	Open	2.8	Open	Open	Open	Open

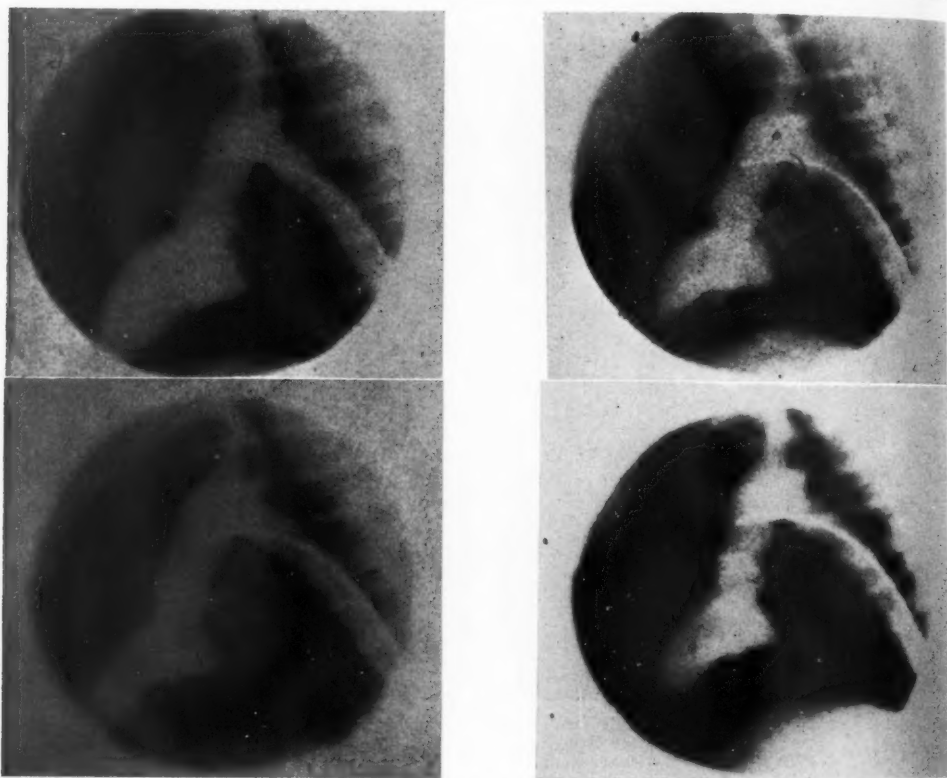


Fig. 6. Cinecardioangiogram of dog heart. The cine frames illustrate the overall image detail obtained on 16-mm. (left) and 35-mm. (right) recordings on Cineflure and Shellburst film.

with dental amalgam of standard U. S. composition:

Ag.....	67-70%
Sn.....	25-27%
Cu.....	0-5.2%
Zn.....	0-1.7%

The amalgam was mixed with mercury in the ratio of 35 per cent amalgam to 65 per cent mercury. The radiograph of this test pattern is shown in Figure 5. The convergent lines of the pattern measure a range of resolution from 15 to 70 line pairs

per inch, and the center line reticle ranges from 14 to 140 line pairs per inch.

With the cameras commercially available, with one Picker 8-inch and one Philips 9-inch cine machine, with lenses of appropriate focal length and aperture so as to record with equal density the entire image of the output phosphor within the film frame, resolution tests were carried out on various popular 16- and 35-mm. film emulsions, with use of the test pattern described above. For comparative purposes, identical tests were run on wire-

screen cloth and the General Electric lead-bar reticle. The types of camera employed and the lens characteristics are given in Table I.

A mere statement of resolving power (the minimal distance two points can be separated and still remain as two points) (5) is not a complete evaluation of the

RESULTS

The results of this study are summarized in Table II. It will be noted that there is a definite gain in image resolution with 35-mm. as compared with 16-mm. film, when the faster coarser-grained film (Cineflure and Tri-X) is used. With finer-grain emulsions (Dupont 140, Plus-X,

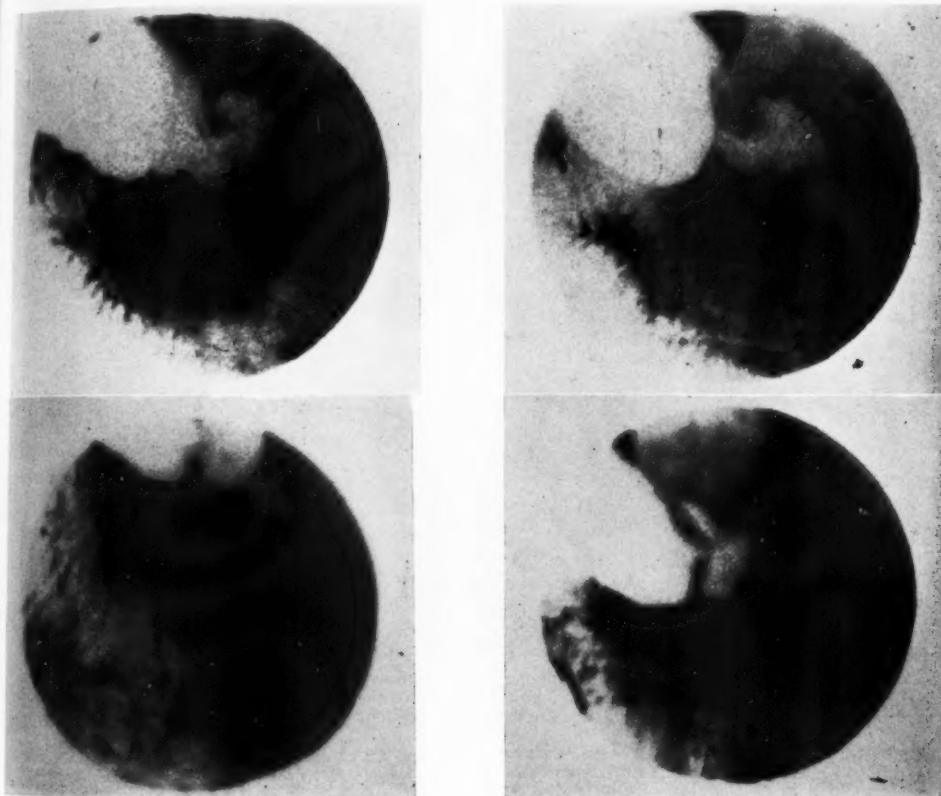


Fig. 7. Gastrointestinal barium study. The cine frames illustrate the image detail obtained on 16-mm. (left) and 35-mm. (right) recordings taken on Cineflure and Shellburst film.

image; the general sharpness of an edge of an object (acutance) (6) is also an important factor. Although the two usually go together, this is not necessarily so. To evaluate this point, cinocardioangiographic (Fig. 6) and gastrointestinal (Fig. 7) studies were recorded on 16-mm. and 35-mm. films, with a fast coarse-grain film of high contrast (Cineflure) and a slower medium-grain high-contrast film (Shellburst).

and Shellburst) this difference is less apparent. It is interesting to note that a medium-grain 16-mm. film such as Shellburst shows resolution similar to that of the coarser-grain 35-mm. Cineflure film emulsion (Fig. 8). On the whole, there is a slightly greater difference in resolution of 35- and 16-mm. film in the Philips system as compared to the Picker. This is thought to be secondary to a 16-mm. lens system of slightly higher resolving power

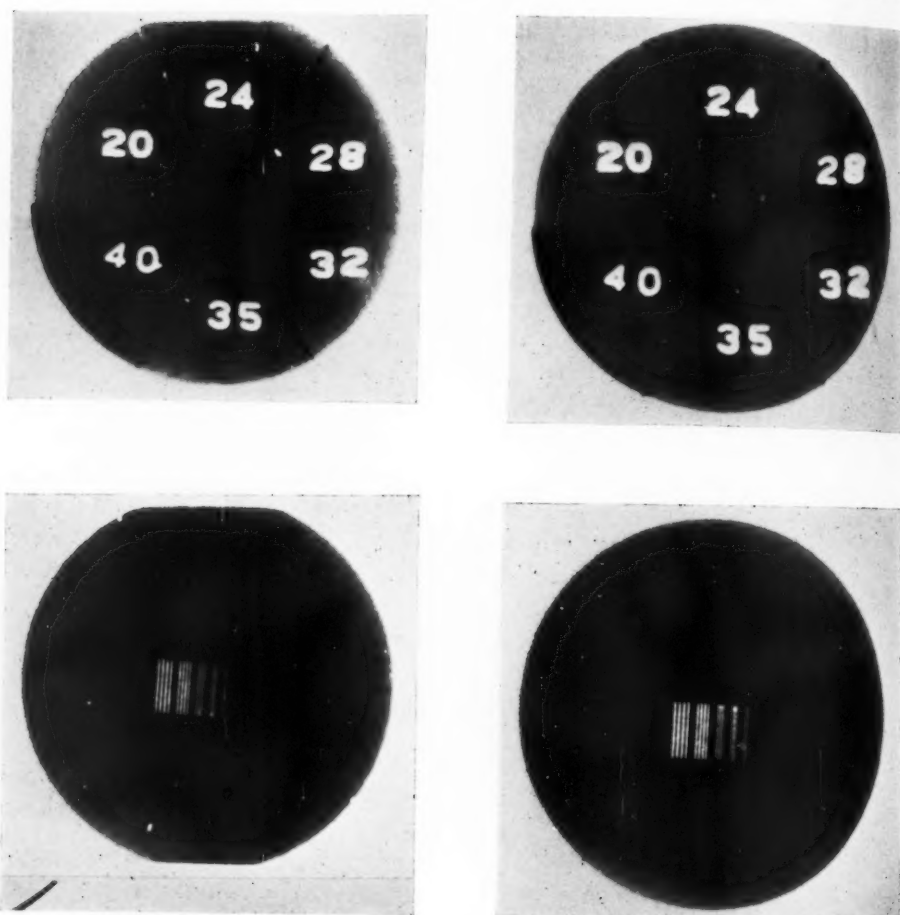


Fig. 8. Comparative resolution of medium and coarse grain film. Although there is considerable loss of detail incident to photographic reproduction, it can be noted that the test patterns resolved by the 16-mm. Shellburst film (left) are similar to those resolved by the 35-mm. Cinefure film (right).

TABLE II: RESOLUTION OF INDIANA UNIVERSITY IMAGE-TUBE TEST PATTERN IN LINE PAIRS PER INCH BY VARIOUS CINEFILM EMULSIONS

Film Type	Maximum Resolution	
	Philips	Picker
Plus-X, 16-mm.	27	35
Plus-X, 35-mm.	32	35
Cinefure, 16-mm.	25	20
Cinefure, 35-mm.	30	35
Shellburst, 16-mm.	27	35
Shellburst, 35-mm.	35	36
Tri-X, 16-mm.	27	27
Tri-X, 35-mm.	30	35
Dupont 140, 16-mm.	30	32
Dupont 140, 35-mm.	35	35

on the Picker system. Although the resolution of the 35-mm. film is similar on the two units tested, the maximum resolu-

tion as observed through the mirror viewer was 40 line pairs per inch on the Philips and 35 line pairs per inch on the Picker.

DISCUSSION

Weinberg (1) and Feddema (7) reported a resolution difference of 10 to 12 line pairs between 16-mm. and 35-mm. films of the same emulsion. Weinberg noted the same improvement in resolution of 35-mm. over 16-mm. films with both fast-speed and medium-grain emulsions. In our studies, in which equal lens speeds on both systems were used, the difference in resolution by 16- and 35-mm. film was less marked and in fact appeared insignificant

in several of the fine- and medium-grain emulsions.

In our own past observations (8), we have been impressed by the improved detail obtained in 16-mm. cinerecordings when the lens aperture is reduced one or two stops. Comparative resolution tests indicate an improvement of approximately 5 line pairs per inch when the camera lens aperture is reduced from $f 0.95$ to $f 2.2$.

In clinical applications we have been unable to appreciate the slight gain in resolution which may be obtained with the use of 35-mm. film. It should be pointed out that we have not utilized fast coarse-grained film in these studies, where a notable difference might have been apparent.

CONCLUSIONS

1. With coarse-grain film emulsions, 35-mm. film resolved as many as 11 more line pairs than 16-mm. film.

2. With medium- or fine-grain film emulsions, the difference in resolution on 16-mm. and 35-mm. film varied from 0 to 3 line pairs per inch.

3. The resolving power of present-day image tubes significantly limits the potential gain in image quality that may be achieved with the use of 35-mm. film.

4. In clinical cineradiography with currently available image intensifiers, the use of medium- and fine-grain 16-mm. film emulsions can be expected to produce images of diagnostic quality equal to that obtained with fast, coarse-grain 35-mm. emulsions for the same radiation dose to the patient.

5. A considerable improvement in image-tube resolution is necessary before the practical advantage of 35-mm. over 16-mm. film will be realized in cineradiography.

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REFERENCES

1. WEINBERG, S., AND WATSON, J. S.: Evaluation of Equipment Films and Processing for Cinefluorography: Cinefluorography. Springfield, Ill., Charles C Thomas, 1960, pp. 91-118.
2. HALLOCK, A., Machlett Tube Corp., Springdale, Conn. Personal communication.
3. BALL, J., Picker X-Ray Corp., Cleveland, Ohio. Personal communication.
4. TER-POGOSSIAN, M., Washington University, St. Louis, Mo. Personal communication.
5. PERRIN, F. H.: Methods of Appraising Photographic Systems. J. Soc. Motion Picture & Television Engineers **69**: 151-156, March 1960; 239-249, April 1960.
6. HIGGINS, G. C., AND PERRIN, F. H.: The Evaluation of Optical Images. Photog. Sc. & Engineering **2**: 66-76, Aug. 2, 1958.
7. FEDDEMA, J.: The Nine-Inch Image Intensifier: Cinefluorography. Springfield, Ill., Charles C Thomas, 1960, pp. 24-34.
8. CAMPBELL, J. A., KLATTE, E. C., AND SHALKOWSKI, R. A.: Factors Influencing Image Quality in Cinerentgenography. Am. J. Roentgenol. **83**: 345-353, February 1960.
- KLATTE, E. C., CAMPBELL, J. A., AND LURIE, P. R.: Technical Factors in Selective Cinecardioangiography. Radiology **73**: 539-546, October 1959.

SUMMARY IN INTERLINGUA

Evaluation del Dimensiones del Pellicula in le Cineradiographia

Le meritos relative del dimensiones del pellicula per se es evaluata como un factor determinatori in le qualitate del imagine cinematic. Es describe un objecto de testage que esseva ideate per le autores pro iste objectivo.

Esseva trovate que in le uso de rapide

pelliculas a grano grossier il occorre un definite ganio de resolution in le imagine quando un pellicula de 35 mm es usate plus tosto que un de 16 mm. Le pellicula de 35 mm resolve usque a 11 plus pares de lineas per pollice que le pellicula de 16 mm. In le uso de emulsiones a grano fin o inter-

mediari, ille differentia variava inter 0 e 3 pares de lineas per pollice. Tamen, le potentia de resolution del currentemente disponibile tubos de imagine restringe significativamente le gano potential in qualitate de imagine que pote esser obtenite con le pellicula de 35 mm.

In le practica del cineradiographia clinic con le currentemente disponibile intensificadores de imagine, il es a expectar que pelliculas de 16 mm con emulsiones a grano

intermediari o fin va producer imagines de un qualitate diagnostic equal a illos obtenite con rapide pelliculas de 35 mm con emulsiones de grano grossier, e isto con le mesme dosage de radiation pro le patiente.

Un considerable melioration del resolution in le tubo de imagines es necessari ante que le avantages del pellicula de 35 mm in comparison con le pellicula de 16 mm pote esser exploitate practicamente.



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Rotation of the Kidney Around Its Longitudinal Axis¹

BELA GONDOS, M.D.²

IT HAS BEEN demonstrated previously (1) that, when a space-occupying force in the abdomen acts in the vertical direction in or close to the plane of the kidney, that organ may respond with rotation around its transverse axis. It is the purpose of the present paper to show that similar physical factors acting in the transverse direction may force the kidney to rotation around its longitudinal axis.

"WIDE PROJECTION" AND "NARROW PROJECTION"

As the result of rotation, the kidney image undergoes significant changes both in size and shape. These changes, if they are of adequate magnitude, can be recognized on the sagittal roentgenogram. For an analysis of the image of the kidney when in rotation around its longitudinal axis, a study of the normal renal image in different projections was undertaken. The calyces and the pelvis were filled by opaque material through the stump of the ureter in order to illustrate changes on the "pyelogram" under the same circumstances (Fig. 1). Two extreme projections were obtained. In broad projection, the kidney casts its true bean-shaped shadow, with a large curvature on its lateral aspect, and shows the concavity of the hilus on the medial aspect. In narrow projection, the concavity of the hilus disappears, the lateral curvature becomes flatter, the superior and inferior extremities have a curvature of shorter radius, and the image as a whole assumes a more symmetrical shape. In its normal environment, the kidney and its adipose capsule are hit by the x-ray beam in a longer diameter when it is in such a position; consequently the kidney image becomes more distinctly outlined.

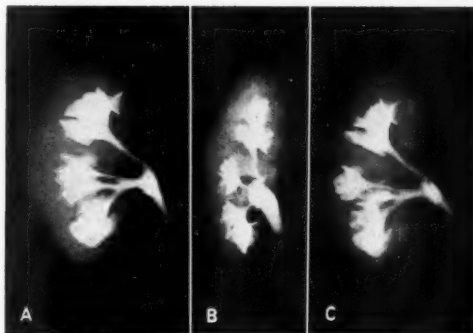


Fig. 1. Kidney removed from the body. A. In broad projection (the hilus looks medially). B. In narrow projection (the hilus faces the x-ray tube). C. In a projection between the two extremes illustrated in A and B.

In a normal person, with the body supine, the kidney ordinarily assumes a position between the two extremes described. There is a "continuous transition" when a larger number of patients is examined. This transition—manifested by the different width and shape in various phases of rotation—can be reproduced and illustrated by films obtained in different angles of obliquity, from one person. The most common "phase of rotation" in which the kidney is found in normal persons is an oblique one, nearer the broad projection. The occurrence of broad projection (without any rotation) is also not uncommon.

Obese persons and males tend to cast an image identical with or near the broad projection. In contrast, undernourished and asthenic persons, as well as females, have a tendency toward the narrow projection (Fig. 2, A). The right kidney image is generally narrower than the left, and the difference is more than is to be expected on the basis of anatomical measurements (2).

¹The material discussed in this paper was a part of a Scientific Exhibit on Physiological and Pathological Rotation of the Kidney, presented at the Annual Meeting of the Radiological Society of North America in Chicago, Ill., Dec. 2-7, 1956. Accepted for publication in September 1960.

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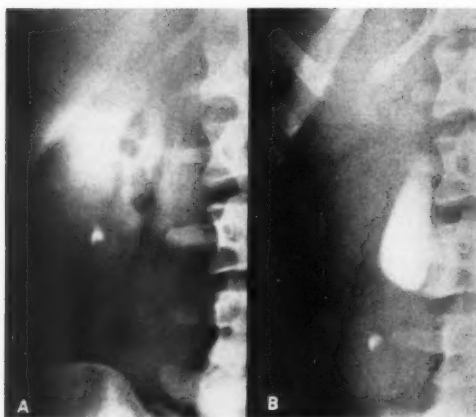


Fig. 2. Roentgenograms of the right kidney of an asthenic woman with a calcific concrement in the inferior calyx.

A. In supine position. The kidney is in an estimated anterior rotation of about 75° .

B. In prone position (cholecystogram). Broad projection. The kidney moved anteriorly to the plane of the psoas muscles. After the elimination of the barrier of the psoas muscles, it moved closer to the midline and rotated with the hilus medially. Compare the narrow projection in the supine with the broad projection in the prone position.

ROTATION AS A RESPONSE TO SPACE ENCROACHMENT

The psoas muscle has an important role in rotation of the kidney around its longitudinal axis. This can be best studied on cross-section anatomical specimens and drawings at different levels of the lumbar segment. The distally increasing mass of the psoas muscle displaces the kidney laterally when it is in ptosis. On the other hand, the renal pedicle and the force of gravity act in the other direction, namely, toward the midline. In other words, the force which tends to move the kidney toward the midline is prevented by the psoas muscle. In this sense, the increasing mass of the psoas muscle in the distal direction manifests itself as a space-occupying factor, to which the kidney has to become adapted. The force thus exerted acts in transverse direction in the frontal plane. Consequently, the kidney will occupy a position with the shortest diameter in this direction after being rotated with the hilus looking anteriorly. In assuming a longer diameter in the sagittal plane, the kidney encounters less resistance by the neighboring ab-

dominal organs. The liver also contributes to the space limitations and is responsible for a more marked rotation and a narrower kidney image on the right as compared with the left.

These observations are made when the body occupies a supine position. In prone position the rotation generally becomes decreased or is eliminated; consequently the kidney casts a wider image (Fig. 2). Increased magnification by the principle of central projection has no significant role in the production of a wider transverse diameter. This is proved by the fact that the length of the kidney image is not affected essentially by the positional change and that the magnification of the second vertebra (which is located in about the same depth as the kidney) was found negligible. Conclusive evidence of the rotation as the cause of the change in the kidney image is provided by lateral films taken with a horizontal beam, with the patient in both the supine and prone position (Fig. 3). This comparative study, utilizing positional changes, well documents the role of the psoas muscle in rotation of the kidney.

An interesting contribution to the mechanism operating in rotation of the kidney is provided by a study of cases of scoliosis. The respective roentgenograms show that the kidney is in narrow projection on the convex side and is in wide projection on the concavity of the scoliosis (Figs. 4-6). On the convex side of the scoliosis, the spine produces a space-occupying effect. It has even been found that there is a gross correlation between the magnitude of scoliosis and the degree of rotation of the kidney. The physical factors on the convexity of scoliosis are similar to those in ptosis: the kidney is forced to engage with the narrowest diameter in the frontal plane and with the longest transverse diameter in the sagittal plane. On the concave side, there is ample space for the assumption of a position with the widest diameter in the frontal plane. In extreme cases an "over-rotation" may occur, with the hilus looking posteriorly (Fig. 6). In this over-rotation



Fig. 3. The kidneys rotate with the hilus medially when the patient is prone. This illustration is presented because of the good and comparable lateral views, particularly on the left. For an explanation of the lateral views, drawings of the right and left urinary passages have been inserted (left dotted; right black).

A. The patient is supine. On the lateral view, obtained with (cross table) a horizontal beam, the left kidney can be identified by its higher position. Note: The left kidney pelvis is projected anterior to the calyces, indicating anterior rotation of the hilus. This kidney is in an estimated rotation of 45° .

B. The patient is prone. The lateral view was obtained with (cross table) a horizontal beam. The left kidney pelvis is projected into the calyces, an indication that it looks medially.

a pulling effect of the vascular pedicle must be a contributing factor.

On the basis of the observations de-

scribed, it may be stated that the kidney rotates around its longitudinal axis as a response to encroachment upon the space

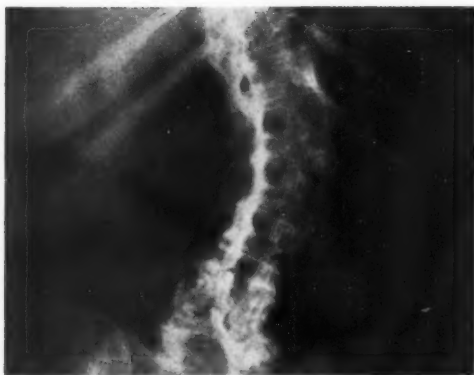


Fig. 4. Rotation of the kidney in scoliosis. The kidney is in a narrow projection on the convexity of the scoliosis and in a wide projection on the concave side. Anteroposterior film of the abdomen.

pressure, and the renal pedicle. Keeping the kidneys in their position, the latter factors either inhibit or modify the rotation produced by the available space (and the force of gravity). The vascular pedicle may contribute to rotation of the kidney by working as a fulcrum, as emphasized by Weyrauch (5).

VALUE OF PRONE POSITION

Broad projection provides more accurate data for evaluation of the actual size and shape of the kidney than different degrees of narrow projection. Consequently, in some cases examination in the prone position could give valuable information if added to the usual film taken in supine

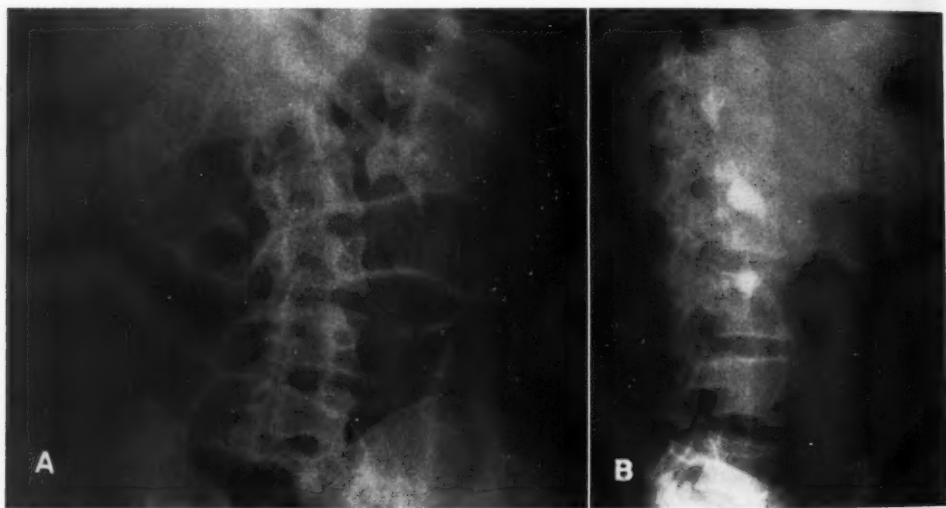


Fig. 5. Scoliosis of lesser degree with corresponding rotation. Intravenous pyelograms in anteroposterior (A) and right lateral (B) positions. The left kidney is in rotation estimated at 45° . The hilus of the right kidney looks medially. (On the lateral film the right kidney can be identified by its lower position. Note: The kidney pelvis is projected into the calyces.) The contour of the kidney images is obscured by the dilated, gas-containing small intestine.

in the frontal plane; *i.e.*, it rotates with the hilus anteriorly in order to adapt itself to the available space. The physical factors playing a part in this rotation can be compared to those acting in rotation of the fetal head in the maternal pelvis during labor. In addition, other factors will affect the rotation of the kidney; these include the size and shape of the kidney bed, the pancreas (on the left side only), the fasciae, the adipose capsule, the intra-abdominal

position. The same applies to measurements of the width of "kidney substance" in hydronephrosis. It seems that measurements with the patient prone would, in many cases, more closely approach the actual anatomical values (4). For better visualization of the renal pelvis in hydronephrosis, it has been suggested that postero-anterior films should also be taken in the respective excretory urographic studies (3). Furthermore, it has been the

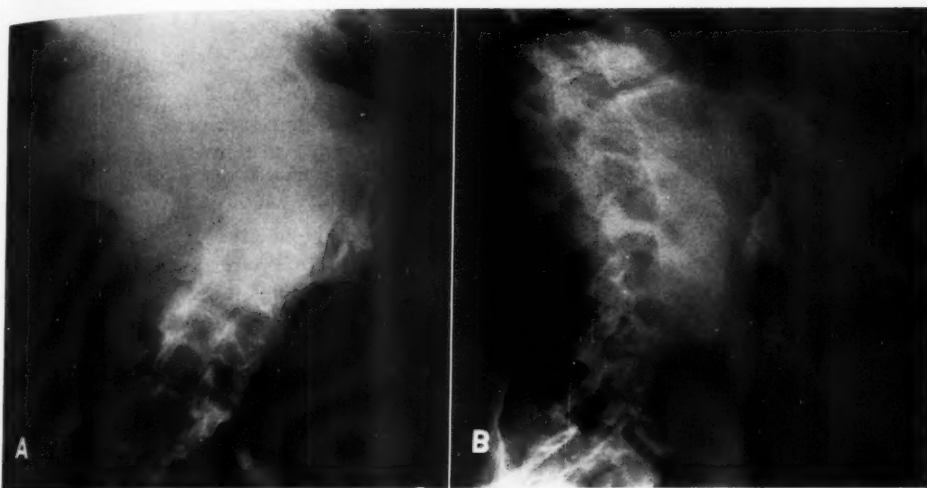


Fig. 6. Marked scoliosis. Excretory urogram. Antero-posterior (A) and lateral (B) views. The right kidney, in the concavity of the scoliosis, is in extreme medial rotation (actually in "over-rotation"). The anteroposterior and lateral views indicate that the kidney pelvis looks medial-posteriorly. Obviously the "pulling effect" of the renal vessels contributed to this rotation. The left kidney, as shown in the anteroposterior view, is in a position consistent with narrow projection; on the lateral view the left upper urinary passages cannot be identified.

author's observation that the upper pole of the kidney is commonly better outlined if the film is taken with the patient prone. Due to rotation in prone position, the kidney may present itself in another view (anteroposterior view in prone; oblique view in supine). Having a second view is in conformity with one of the basic requirements in diagnostic roentgenology.

SUMMARY

1. When the patient is supine, the kidney tends to rotate, with the hilus anteriorly, as a response to diminished space in the frontal plane lateral to the psoas muscle. This rotation is more marked on the right side than on the left. In scoliosis similar rotation may occur on the side of the convexity, while on the concave side the hilus of the kidney rotates medially.

2. When the patient is prone, the kidney tends to occupy a position identical with or near the broad projection.

3. As the result of rotation there is a change in the kidney image. When the

hilus looks anteriorly the kidney image is narrower and more symmetrical in shape. When the hilus is on the medial aspect the kidney image is wider and of the usual bean shape.

4. The wide projection may more closely approach the anatomical values of the kidney in respect to size and shape than the usual projection in the supine position. The same applies to evaluation of the width of the kidney parenchyma on pyelograms or urograms.

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REFERENCES

1. GONDOS, B.: Rotation of the Kidney Around Its Transverse Axis. *Radiology* 74: 19-25, January 1960.
2. GONDOS, B.: Roentgenographic Evaluation of the Size and Shape of the Kidney. To be published.
3. McLAUGHLIN, W. L., AND BOWLER, J. P.: Excretory Urography in the Diagnosis of Ureteropelvic Obstruction. *J. Urol.* 67: 1012-1016, June 1952.
4. ROBINS, S. A., AND FISCHMANN, J.: Hydronephrosis. A Radiological Classification Based on Anatomical Variations. *Radiology* 50: 632-638, May 1948.
5. WEYRAUCH, H. M., JR.: Significance of Renal Torsion in Diagnosis of Retroperitoneal Tumors. Use of Lateral Pyelogram. *J. Urol.* 41: 877-892, June 1939.

(Pro le summario in interlingua, vider le pagina sequente)

SUMMARIO IN INTERLINGUA

Rotation del Ren Circum Su Axe Longitudinal

Quando le patiente es in decubito dorsal, le ren tende a rotar se anteriormente con le hilo, in responsa al reduction de spatio in le plano frontal, lateral al musculo psoas. Iste rotation es plus marcate al latere dextere que al latere sinistre. In scoliosis, un simile rotation occorre a vices al latere del convexitate, durante que al latere del concavitate le hilo del ren es rotate medialmente.

Quando le patiente es in decubito ventral, le ren tende a occupar un position identic o quasi identic con le "projection large." In iste projection le ren jecta su ver umbra fabiforme con le grande curvatura al aspecto lateral.

Como resultado del rotation il occorre un alteration in le imagine del ren. Quando le hilo reguarda in direction anterior, le imagine del ren es minus large e plus symmetric in conformation. Quando le hilo occupa le aspecto medial, le imagine del ren es plus large e exhibi le usual conformation de un faba.

Le projection large es capace a approchar plus plenmente le valores anatomic del ren con respecto a su dimension e conformation que le usual projection in decubito dorsal. Le mesme considerationes vale pro le evaluation del largor del parenchyma renal in pyelogrammas o urogrammas.



A Method and Parameters for the Analysis of Renal Function by External Scintillation Detector Technic¹

RICHARD L. WITCOFSKI, M.S., JOSEPH E. WHITLEY, M.D., I. MESCHAN, M.D.,
and CAPT. WILLIAM E. PAINTER, USAF (MC)

THE IODOPYRACET renogram (i.e., the graphic record of kidney excretion) has been a useful clinical tool, but its utility in evaluation of renal function is limited because of hepatic interference. With the advent of more selective agents, as ortho-iodohippuric acid I¹³¹ (OIHA)², hepatic uptake has been minimized (1). It is now possible to compare right and left renal curves with greater confidence, and theoretically to produce quantitative values related to renal function. With such values it should be possible to define limits of normal function.

METHODS OF RENOGRAM ANALYSIS

The analysis of the renogram can be approached in four possible ways:

I. A Visual Comparison of the Curves: In this method the curves are compared as to height and shape by observation. The *advantage* of the method is that the analysis can be completed quickly and requires only a trained interpreter. The *disadvantages* are: (a) that a rather broad experience in renogram interpretation is required; (b) that interpretation is difficult when only one kidney is functioning; (c) that the height of the complex and its visual presentation are affected by the distance, the dose, the time constant, and the chart recorder speed.

II. A Comparison with Group Envelopes: With this method, several normal curves are plotted and an envelope drawn which includes all these curves. The *advantage* of this method is that results may be analyzed quickly. The *disadvantages* are:

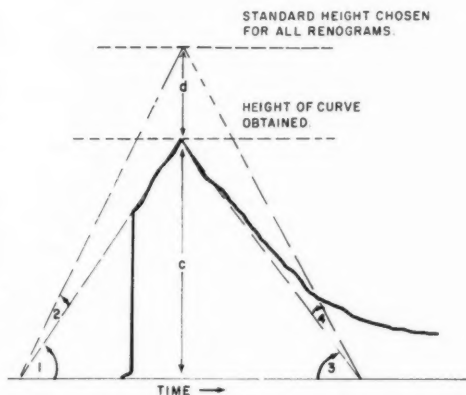


Fig. 1. Use of the angle of rise and decline in the renogram to quantitate the rate of secretion and excretion. The curves must be corrected to a standard height as shown.

(a) that all curves must be standardized to the same height; (b) that the method does not allow complete description of normal function; (c) that quantitation of the degree of abnormality is not possible; (d) that individual standardization is required with different equipment.

III. Angles and Tangents: This procedure utilizes the slopes of increase and decrease (measured as an angle or its tangent) as a measure of the rapidity with which the kidney is concentrating and excreting the radioactive material. The curves must be extrapolated to the same height with either method. Figure 1 shows a typical renogram. The maximum height obtained was c . However, the "standard height" chosen is $c + d$. Angle 1 measures the secretory slope and angle 2, the excretory slope of the original

¹From the Department of Radiology (R. L. W., Physicist; J. E. W., Fellow in Radiological Research of the James Picker Foundation; I. M., Professor and Director; W. E. P., Assistant Resident), Bowman Gray School of Medicine and the North Carolina Baptist Hospital, Winston-Salem, N. C. This project was supported by the North Carolina Heart Association; H. T. S. 5392, National Institutes of Health; National Institutes of Health Pancreas Grant C-3026. Presented at the Forty-sixth Annual Meeting of the Radiological Society of North America, Cincinnati, Ohio, Dec. 4-9, 1960.

The contents of this article represent the personal views of the Air Force author and are not to be construed as a statement of official Air Force policy.

²"Hippotope," from E. R. Squibb & Sons, New York, N. Y.

curve. These may be extended to the "standard height" by drawing them as shown. Angle $1 + 2$ represents the secretory slope while angle $3 + 4$ represents the excretory slope. The values may also be expressed as the tangents of the angles. To extend these to the standard heights the tangents of angles 1 and 3 must be multiplied by $(c + d)/c$.³

The advantage of this method is that it affords some descriptive indication as to degree of normality or abnormality.

half-secretory and excretory times for each kidney curve (3) and half-clearance times for the blood. On the basis of the blood curve, the activity of the blood sample, and the bladder activity, blood clearance can be calculated.

The advantages of this method are: (a) that an expression of renal blood inflow may be obtained; (b) that factors expressing the rate and amount of secretory and excretory work may be derived; (c) that these values may be used to compare

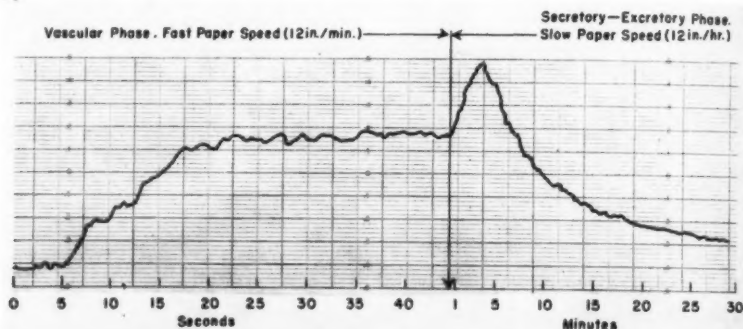


Fig. 2. A normal renogram tracing illustrating the use of the fast paper speed and time constant for the vascular phase, with the remainder of the curve run at a slow speed.

The disadvantages are: (a) that it is difficult to draw a straight line which closely represents a curve of an exponential nature; (b) that variability between machines will affect normal values.

IV. Proposed Method: In the proposed method, the recorder is run at a fast paper speed and time constant until activity levels over the kidneys reach a plateau (2). At this point the paper speed is decreased and the renogram is completed. A typical curve is shown in Figure 2. A chart recording is also made of the blood activity with a third probe. A venous blood sample is obtained and the percentage of the total dose in the bladder is determined at thirty minutes.

The mean and the plateau times of the vascular phase are determined, as are

and describe populations statistically; (d) that clearance may be obtained.

The disadvantages are: (a) that curves must be replotted on a semilogarithmic scale though this step may be obviated with the introduction of semilog recorders; (b) that the test is more time-consuming and requires a venipuncture.

EQUIPMENT

The unit consists of matched collimated probes ($1\frac{1}{2} \times 1$ -inch NaI (T1) crystals), matched ratemeters, and a dual rectilinear chart recorder. The crystals are recessed 7.0 cm. from the face of the cone, with a cone aperture of 8.4 cm. In Figure 3 is shown a polar plot of this crystal-collimator combination for iodine 131. The solid angle "seen" by the crystal is fairly large, and this is felt to be advantageous, since it helps preclude the possibility of "missing" the kidneys due to errors in positioning. This large angle may be a disadvantage in children.

³ In 20 normal medical students ortho-iodohippuric acid I^{131} renograms were obtained. With this method of analysis, the following values were recorded:

(1) Secretory angle = $60.3^\circ \pm 8.3^\circ$
 (2) Excretory angle = $55.0^\circ \pm 9.0^\circ$
 (Standard height of 0.9 full-scale deflection)

The third probe used is a collimated 2 X 2-inch NaI (T1) crystal connected to a spectrometer-ratemeter-recorder combination. Marginal timer markers operating from one synchronous timer are provided for both the single and dual channel recorders.

METHOD OF TESTING

The proposed method of testing may be summarized as follows:

1. The position of the kidneys is deter-

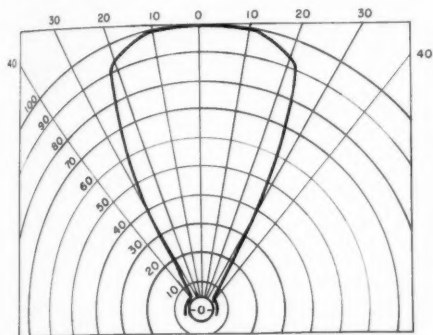


Fig. 3. A response curve with the probe-collimator combination for I^{131} .

mined either by an erect scout film of the abdomen, or from a small amount of the tagged material (2 to 5 microcuries) with probe localization. The first procedure is preferred.

2. A dose of 1 $\mu\text{C}/3$ kg. containing 2 to 4 μg . of OIHA per μC (4), is standardized against a 20 μC "mock iodine" source.

3. The patient empties his bladder prior to injection.

4. The kidney probes are balanced for equal response and placed perpendicular to the back, over the respective renal areas.

5. The third probe is positioned over the umbilicus.

6. The chart recorders are started, and a rapid intravenous injection of the dose of OIHA is made, through a No. 20 needle.

7. The dual chart recorder is run at a fast paper speed (12 in./min.) and fast time constant (0.5 sec.) until the activity

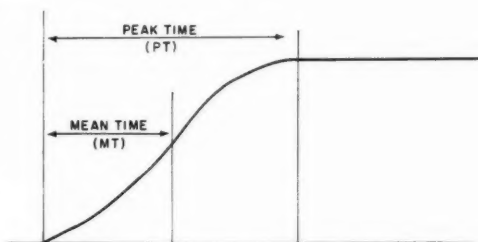


Fig. 4. The mean vascular and plateau times (PT) of the vascular phase.

level reaches a plateau (usually 0.5 to 1 min.). The dose should be sufficient to yield at least half of full-scale deflection.

8. When the bolus shape has been recorded by the probe over the umbilicus, the probe is moved over the sternum and angled cephalad to avoid "seeing" the kidneys.

9. After the initial vascular segment, the chart speed of the rectiwriter is changed to 12 in./hr. and the curves are recorded until the excretory slopes reach a plateau.

10. The blood activity is followed until a plateau is reached. At that time a blood sample is drawn and the time of sampling is noted.

11. At thirty minutes the patient is placed supine. The third probe is then placed over the bladder (40 cm. distance) and a count is obtained. A circular lead shield (2 cm. thick with a diameter of 15 cm.) is then placed over the bladder, and a "background" count is obtained.

12. The syringe used for injection is counted against the standard, and the amount of residual I^{131} is determined.

13. The mock iodine standard is counted in the pelvic phantom.⁴

ANALYSIS OF DATA AND RESULTS

The Vascular Phase: The three parameters are: (a) the respective appearance times of the OIHA in each kidney; (b) the time increment from the initial influx of

⁴ To measure the urine activity *in vivo*, an 18 X 22-cm. Presdwood pelvic phantom was constructed according to Eycleshymer and Schoemaker. (5). A central bladder point was selected 6 cm. below the anterior surface of the phantom. The "mock iodine" standard is routinely counted in this position.

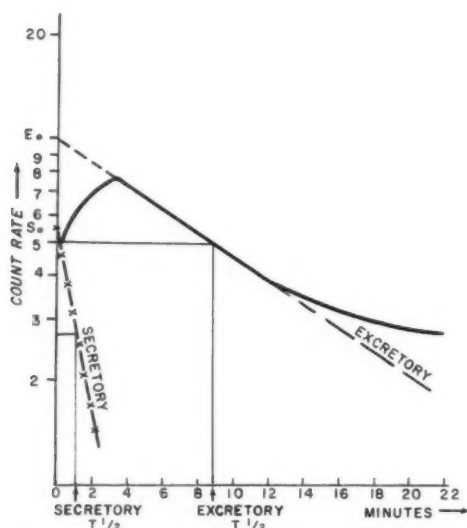


Fig. 5. An example of a renogram curve replotted on a semilogarithmic scale, demonstrating the determination of the half-secretory and half-excretory times.

activity to the origin of the plateau, the plateau time (PT); (c) the mean vascular time (MVT) (Fig. 4), obtained with a planimeter from area measurements.

Table I lists the values obtained for these parameters in 20 normal medical students (average age 24.2 years).

TABLE I: VALUES OBTAINED FOR THE VASCULAR PHASE OF THE RENOGAM

Kidney	MVT and Standard Deviation in Seconds	PT and Standard Deviation in Seconds
Right	12.1 ± 5.5	24.8 ± 10.4
Left	10.2 ± 4.4	22.4 ± 10.3

The mean of the individual differences between the MVT's (ΔMVT) of the right and left kidneys is 1.89 ± 0.49 sec. with the mean time on the left side always equal to or shorter than that on the right. The probability of this difference occurring by chance was calculated to be less than five in one thousand ($P < 0.005$). The mean of the individual differences in the plateau times (ΔPT) between the two kidneys was 2.33 ± 1.76 sec. This difference, however, was not significant ($0.4 > p > 0.2$). The difference in the

mean vascular times is most probably due to an asymmetry in the vascular anatomy "seen" by each probe.

The Secretory-Excretory Phase: The remainder of the curve following the vascular phase is replotted on semilogarithmic paper (Fig. 5). The excretion line (E), which most closely follows the excretory slope, is drawn and extended to intersect the ordinate at E . The secretory line (S) is obtained by plotting the differences between line E and the rising secretory

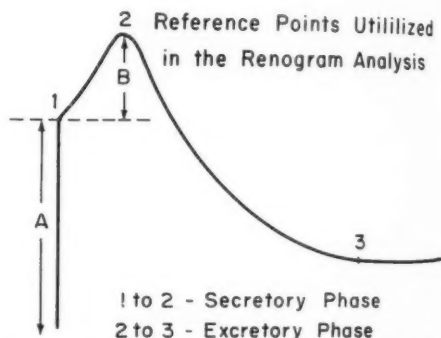


Fig. 6. A renogram curve with the heights B and A shown.

phase of the renogram curve. These points are connected by a straight line to intersect the ordinate at S_0 . The secretion half-time ($ST 1/2$) is the time increment between the beginning of the secretory phase and $S = 1/2 S_0$. The excretory half-time ($ET 1/2$) is the time between E_0 and $E = 1/2 E_0$.

Figure 6 demonstrates the portions of the curve with the heights B and A . A is the height of the vascular plateau and B is the height of the curve above the plateau.

The Blood Curve: The blood curve (B) is also plotted on semilogarithmic paper (Fig. 7). The blood level at thirty minutes is extrapolated back to time zero and the extrapolated curve (BE) is subtracted from the descending blood curve (B). The difference is plotted as BD and extended to the ordinate at B_0 . A blood removal half-time ($BT 1/2$) is when $BD = 1/2 B_0$. A blood sample is obtained at

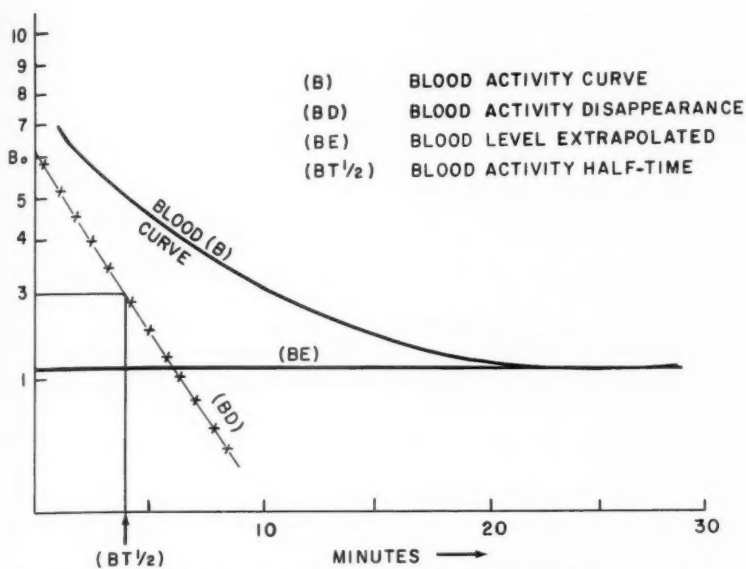


Fig. 7. A semilogarithmic plot of the blood curve demonstrating the removal rate ($BT^{1/2}$).

thirty minutes, and counted in a scintillation well counter. From the blood aliquot activity and the blood curve, the blood activity at any time may be determined. This value is required in the calculation of clearance rates.

Urine Activity: The urine activity is calculated as:

$$\text{percent of injected dose in the urine} = \frac{B - S}{R}$$

where:

B = bladder activity in counts/min.

S = activity with shield in counts/min.

R = per cent of the standard injected \times counts/min. of the standard in the phantom.

In comparing the values obtained with this *in vivo* method to those from voided samples, the only errors encountered were demonstrated to be due to incomplete bladder emptying.

Normal values for the secretory-excretory parameters are listed in Table II.

Clearances: Clearance determinations were calculated by the classical formula:

$$\text{Clearance} = UV/P$$

TABLE II: NORMAL VALUES FOR THE RENAL FUNCTION PARAMETERS DESCRIBED ($N = 20$)

Parameter	Value and Standard Deviation	Range of 2 Standard Deviations
Secretory half-time	1.4 ± 0.5 min.	0.4 to 2.4 min.
Excretory half-time	8.1 ± 2.7 min.	2.7 to 13.5 min.
Blood half-time	4.4 ± 1.5 min.	1.4 to 7.4 min.
Percentage excretion at 30 min.	$58.6 \pm 10.4\%$	37.8 to 79.4%
Peak time	3.8 ± 1.2 min.	1.4 to 6.2 min.
B/A	0.58 ± 0.23	0.12 to 1.04

Where U is the concentration of the substance per cubic centimeter of urine, V is the total urine volume, and P is the plasma concentration per cubic centimeter.

The percentage measured at thirty minutes in the bladder was felt to afford a more accurate estimation of UV than the voided specimen, since it excludes the problem of incomplete voiding. The blood concentration measured from the blood specimen was extrapolated to a mean value, employing the blood curve.

The values encountered ranged from 128 to 498 c.c. per minute, with a mean plasma clearance of 234 ± 145 c.c. per

minute (corrected to 1.73 square meters surface area).

DISCUSSION

The principal component of the vascular phase of the renogram is due to high flow within the renal vascular bed and its relative proximity to the probe. After nephrectomy, a vascular curve is recorded, indicating an extrarenal contribution to the renogram. This component, however, is small and relatively constant and does not limit the scope of the test. Interpretation of a vascular phase not followed by recognizable evidence of renal function or a vascular phase of less than half of full-scale deflection makes the ΔMVT and ΔPT measurements questionable. In such cases, interpretation of the relative heights of the vascular plateaus may be meaningful.

The absolute appearance time is theoretically affected only by near-complete occlusion of the renal artery. In such cases, the background vascularity may mask this delay.

The ΔMVT and ΔPT reflect the differences in the blood flow of the renal vascular tree. The normal variations in ΔMVT and ΔPT are defined, and significant variations from the norms are indicative of unilateral renal arterial or arteriolar disease. The differences in the mean vascular times (ΔMVT) and the plateau times (ΔPT) between the two kidneys are independent of the bolus. The MVT and the PT are dependent both on the shape of the bolus that reaches the renal arteries and the presence or absence of irregularities in caliber of the vascular tree.

Bolus shape is dependent upon the speed and volume of injection, partial or complete extravasation, the rate of flow in the vein injected, the central blood volume, the cardiac output, intracardiac shunts, and vessel irregularity proximal to the renal arteries. However, with the small injection volumes (<0.5 c.c.) employed in our series, the bolus shape has been consistent (Table I). In order to compensate for bolus differences in an unknown population, it is necessary to

view the bolus presented to the renal arteries. With the described approach, it should be possible to detect bilateral renal artery disease.

Secretory Phase: The secretory half-time ($ST\ 1/2$) is a measure of the rate of concentration of the OIHA by the kidney tubules. The parameter B/A measures the concentration above the vascular level and is a function of renal work. The peak time (point 2 on Fig. 6) is that time at which the rates of secretion and excretion are balanced. The blood half-time ($BT\ 1/2$) is a measure of the speed with which the kidneys are concentrating the OIHA.

Excretory Phase: The excretory half-time ($ET\ 1/2$) is a measure of the rate at which the OIHA is removed from the kidneys. Percentage excretion at thirty minutes is a measure not only of excretion but also of total renal work.

Clearance: The clearances obtained are of the single dose type without an antecedent equilibration period. Utilization of this technic on persons who are not in a basal state resulted in low clearance values with a large standard deviation. With repetition of the procedure in the same individuals with more effort toward attainment of a basal state, greater values of clearance would undoubtedly be encountered.

Classical clearances could be performed with an intravenous drip of nonradioactive OIHA or similar selective compounds in persons in a basal state. This would involve superimposition of insignificant single doses of radioactive OIHA upon an equilibrated state of renal function. The described technic, without bilateral ureteral catheterization, should give classical clearance results. The correlation of the other parameters with traditional tests of renal function (tubular maximum, functional tubular mass, etc.) should be possible.

CONCLUSIONS

(1) A procedure for obtaining renograms is presented, with acceleration of the vascular phase and determination of blad-

der and blood radioactivity at thirty minutes.

(2) A technic of analysis is proposed, disassociating the vascular phase and the secretory-excretory phase. This method is compared to others commonly employed.

(3) Parameters expressing the rates of secretion and excretion and total renal work are outlined. A method of performing clearance studies and its possible further applications are discussed.

(4) Normal values for the suggested parameters including acute clearance studies are presented for ortho-iodohippuric acid.

(5) This procedure affords a new approach to the estimation of renal blood flow.

REFERENCES

1. WHITLEY, J. E., WITCOFSKI, R. L., AND MESCHAN, I.: Experimental Comparison of Ortho-Iodohippuric Acid and Iodopyracet in Renal Function Evaluation. *Radiology* **76**: 464-466, March 1961.
2. MAGNUSSEN, G.: The Distribution of ^{131}I -Diodrast Studied with Autoradiography. *Acta med. scandinav.* **166**: 35-41, Jan. 25, 1960.
3. BLOCK, J. B., HINE, G. J., AND BURROWS, B. A.: Effects of Carrier Diodrast on Excretion of ^{131}I -Labeled Diodrast. *J. Lab. & Clin. Med.* **56**: 110-119, July 1960.
4. Personal communication, E. R. Squibb & Sons.
5. EYCLESHYMER, A. C., AND SCHOEMAKER, D. M.: *A Cross Section Anatomy*. New York, D. Appleton & Co., 2d Ed., 1930.
6. NORDYKE, R. A., TUBIS, M., AND BLAHD, W. H.: Simultaneous Comparison of Individual Kidney Function using Radioiodinated Hippuran. *Clin. Res. Proc.* **8**: 116, January 1960.
7. TUBIS, M., POSNICK, E., AND NORDYKE, R. A.: Preparation and Use of ^{131}I -Labeled Sodium Iodohippurate in Kidney Function Tests. *Proc. Soc. Exper. Biol. & Med.* **103**: 497-498, March 1960.

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DISCUSSION

Henry Plenk, M.D. (Salt Lake City, Utah): I didn't get the number of cases.

Dr. Whitley: The normal values I quoted were obtained in 20 medical students. We have a patient series which is much larger, including 24 "normal" patients. Actually we have applied the procedure in over 200 clinical cases of various and sundry conditions.

Rosalyn S. Yalow, Ph.D. (New York): Was the slower rate of disappearance of the radioactivity from the blood at the end of the half-hour due to contamination with labeled material other than the labeled dye?

Dr. Whitley: We have not investigated the purity of our compound. We use the commercial preparation put out by the Squibb Company.

Dr. Yalow: How do you account for the slow rate of disappearance?

Dr. Whitley: One can assume that the kidney cleared the material at different rates depending upon the plasma level; or that there was more than one process affecting the disappearance curve.

Louis Katz, M.D. (New York): The reason why there is a slow disappearance of activity on the renogram is that, after a single injection, Hippuran or PAH goes into the interstitial fluids as well as being excreted by the kidney. Prolonged activity measured over the kidney is due to the Hippuran leaving the interstitial fluids.

This is also a major criticism of this technic for performing renal clearance of any substance. When a substance is first injected, clearance from the plasma occurs both through the kidneys and into the interstitial fluids. After equilibrium occurs between the plasma and fluid, one has the additional complicating factor of a return to the plasma of the substance as it is cleared by the kidney.

Dr. Whitley: Yes, I believe this does occur with OIHA and there is also some plasma protein binding and disassociation as an additional factor.

R. R. Newell, M.D. (San Francisco, Calif.): I want to express my appreciation of a nice, brief, sharp exposition, to the point.

(Pro le summario in interlingua, vider le pagina sequente)

SUMMARIO IN INTERLINGUA

Un Methodo—e le Parametros in Illo—pro le Analyse del Function Renal per Medio de Technicas Externe de Detection Scientillatori

Es presentate un technica pro le obtention de renogrammas, con acceleration del phase vascular e determination del radioactivitate in vesica e sanguine post trenta minutas. Es usate un dual registrator cartographic rectilinee que es activate a alte velocitate de papiro usque le radioactivitate supra le ren attinge un plateau. Allora le velocitate de papiro es reduce, e le renogramma es completate. Un graphico es facite in que le activitate in le sanguine es registrate per medio de un tertie sonda. Un specimen de sanguine venose es obtenite e le procentage del dose total del isotopo in le vesica es determinate post trenta minutas. Le tempore medie e le tempore pro le plateau in le phase

vascular es determinate, si ben como le tempores de medie-secretion e de excretion pro le renes individual e le tempore de medie-clearance pro le sanguine. Super le base del curva pro le sanguine, del activitate in le specimen de sanguine, e le activitate in le vesica, le clearance sanguinee pote esser calculate.

Parametros que exprime le proratas de secretion e de excretion e le travaglio renal total es delineate. Valores normal pro le proponite parametros—incluse studios de clearance acute—es presentate pro acido orthiodohippuric.

Iste technica representa un nove tactica in le estimation del fluxo de sanguine renal e le detection de morbo de arteria renal.



Differential "Nephropacification": A Screening Procedure for Unilateral Renal Artery Occlusion¹

JOHN C. RATHE, M.D.²

DIFFERENTIAL renal opacification during intravenous aortography has been found to indicate unilateral ischemia secondary to occlusive renal artery disease. The nephrogram is directly related to renal blood flow when no collecting system obstruction pre-exists, and a kidney with poor blood supply will show diminished nephrographic density. The intravenous method is thought to be more sensitive and certain for nephrography and also more applicable as a screening procedure in routine practice than translumbar aortography or the radioactive iodine renogram.

The nephrogram is the representation on film of kidney parenchyma made radiopaque by its accumulation of contrast material. The pyelogram, created by contrast filling of the calyceal system, is a subsequent phase of concentration and collection of the excreted medium. The normal excretory pyelogram resulting from conventional technics will not show appreciable increase of parenchymal density. Dense renal opacification is created only when blood heavily laden with contrast medium courses through the renal circulation, simultaneously entering the glomerular filtrate and the tubular cells. Radiodensity so produced will be referred to in this paper as "nephropacification" in preference to the less direct term "nephrogram effect," which is often used.

Nephropacification has been clinically useful for many years (12), being noted in association with ureteral obstruction and hypotension (3), as well as constituting an important part of the angioneurotomographic technic of Evans, Dubilier, and Montieth (4).

A previous observation of differential nephropacity effect was made by Liese as

a part of the angiotomographic technic for visualization of the visceral arteries (8). Intravenous aortography was also used in this procedure. Liese reported 4 cases of renal artery occlusion due to arteriosclerotic plaques; in all of these there was deficient nephropacity of the affected kidneys (Fig. 4). A fifth instance of this phenomenon is furnished by the following case.

CASE REPORT

F. C., a 42-year-old white single female, was recently admitted to the San Francisco Veterans Administration Hospital with a history of hypertension of four months duration. Prior to that time she had been normotensive. The past medical history was otherwise noncontributory. Initial blood pressures in the range of 220/110 could be reduced to 175/95 with antihypertensive therapy or bed rest.

Pre-admission excretory urography showed the right kidney to be significantly smaller than the left, but function seemed normal. A repeat study with a film at three minutes yielded a poor pyelogram on the right; by seven minutes the concentration and calyceal filling on the right approximated that on the left (Fig. 1). Intravenous aortography showed a dense nephrogram on the left and little opacification on the right (Fig. 2, A). The primary arterial lesion, with stenosis and post-stenotic aneurysm, was demonstrated in the midportion of the right renal artery by a translumbar aortogram (Fig. 3).

Laboratory findings, including urinary catecholamines, were within normal limits. The differential renal excretory tests could not be considered abnormal because of leakage around the catheters.

At surgery the offending segment of renal artery was excised and an end-to-end anastomosis was performed. Pathologic diagnosis was medial fibromuscular hyperplasia. Bilateral renal biopsies were normal.

One week postoperatively the right renal artery was demonstrated to be patent by an intravenous aortogram (Fig. 2, B). The nephrogram and early pyelogram on the right showed improvement in comparison with similar preoperative studies. Three weeks after operation the blood pressure was 135/80. It is still normal nine months later.

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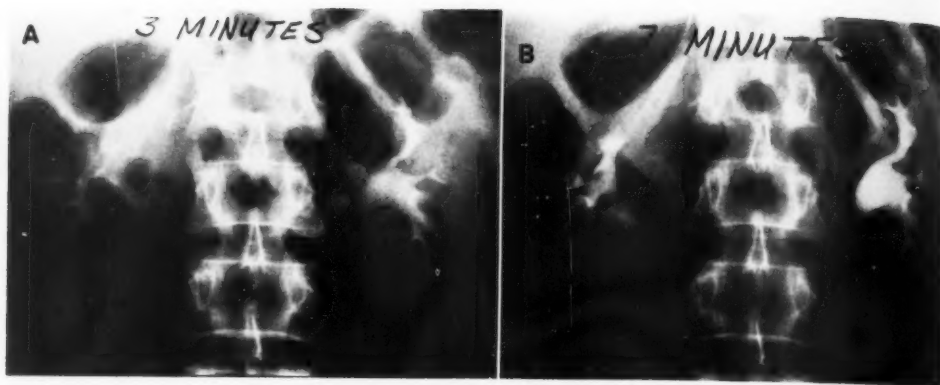


Fig. 1. F. C. Preoperative excretory urograms.

- A. Three-minute film demonstrating poor calyceal filling on the right.
 B. Seven minutes after injection, the density of the pyelogram on the right is very nearly equal to that on the left. Right kidney is smaller than the left.

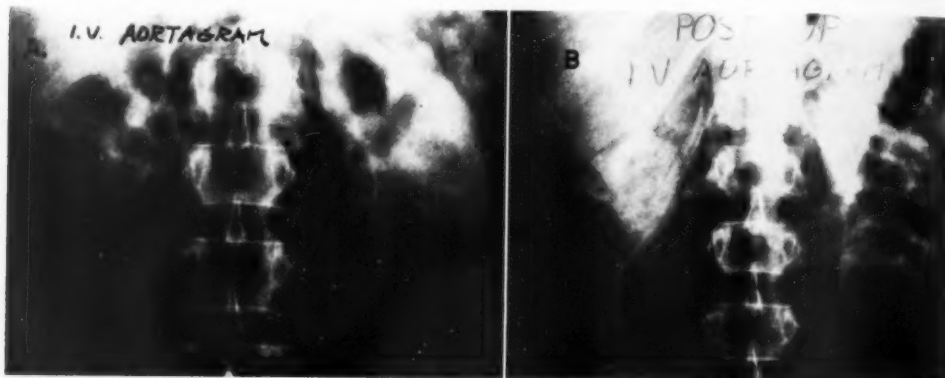


Fig. 2. F. C. Intravenous aortogram.

- A. Before operation. Note poor nephropathy on right, dense nephropathy on left.
 B. One week after excision and re-anastomosis of the right renal artery, shown to be patent on this study. Improvement of circulation and nephropathy on right.

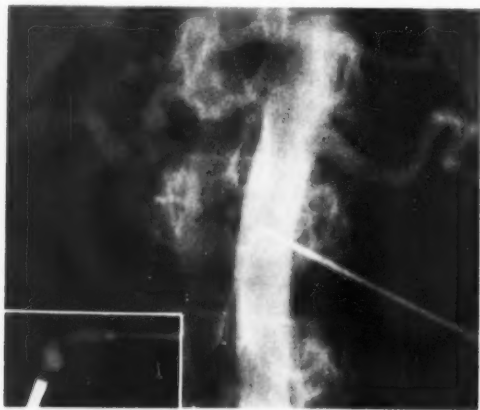


Fig. 3. F. C. Translumbar aortogram. Stenotic area with post-stenotic aneurysm visualized. The insert shows the injected surgical specimen.

TECHNIC

The methods employed in the above case parallel those generally used for intravenous aortography (5). A 15-gauge needle with two-way stopcock was inserted in each antecubital vein. Thirty cubic centimeters of 85 per cent Hypaque was rapidly and simultaneously injected into each arm. The important immediate film of the abdomen was taken with a three-second exposure beginning just at the arm-to-tongue circulation time as determined with Decholin. This can be followed serially with pyelographic films at one, three, and seven minutes.

Optimal technic for this type of study

includes use of two 12-gauge needles and injection of 40 c.c. of 85 per cent contrast material through each for a total dose of 80 c.c. The renal arteries as well as the nephropacity of each kidney can be demonstrated especially well with polytomography, in the arteriographic phase.

As a simple but effective screening procedure, the following modification will suffice for demonstrating differential nephropacity. Ordinary urographic contrast medium (50-55 c.c.) is injected as rapidly as possible through a 15-gauge needle into the medial antecubital vein. A single flat film of the abdomen is obtained approximately fifteen seconds later for patients believed to have a normal circulation time. An example of this



Fig. 5. Normal nephrogram. Plain film of abdomen taken fifteen seconds after rapid intravenous injection of 50 c.c. of 50 per cent Hypaque through one 15-gauge needle.



Fig. 4. Abnormal nephrogram. Arteriosclerotic plaque occluding left renal artery shown by tomography.
A. Arterial phase: no nephropacification on left.
B. Forty-five second film: minimal opacification developing.

method is shown in Figure 5. The use of Decholin and of heavily concentrated contrast materials is optional, as is tomography.

DISCUSSION

The vascular and parenchymal components of nephropacity were defined by Edling and Helander (2). Contrast filling of arteries and capillaries lasts only as long as blood carrying the medium remains in the renal artery. Within seconds the capillaries are emptied of this blood, and the iodide filtered into the tubules or trapped

by the tubular cells provides a more intense opacification. This persists ten to twenty seconds and then is gradually lost as the contrast agent flows out the renal vein or down the tubules in the urine. Thus, the nephrogram begins with arterial contrast filling but the most intense opacification will result soon thereafter from filtration and excretion of the medium.

Differential nephropacification may be invalidated by the presence of contrast medium in the kidney prior to the bolus study. The maximum opacity is obtained when a bolus of iodide enters the renal

artery rapidly and filming is begun shortly thereafter. Filtration and tubular accumulation of the medium take place slowly in the ischemic kidney. Unless there is complete vascular occlusion and loss of function, the ischemic kidney is slowly "loaded" by the recirculation of iodide during clearance from the blood. Figure 4, B demonstrates this delayed appearance of nephropacification. Apparently normal density could result from the cumulative contrast due to slow excretion of a preliminary dose and the inadequate amount passing the narrowed renal artery.

The cause of diminished nephropacity in a nonpyelonephritic kidney is readily understood in light of the preceding discussion. The volume of contrast-laden blood which can pass through a constricted renal artery at a given pressure will diminish with the shrinking diameter of the vessel. This volume is in effect recorded on the immediate nephrogram before recirculation of the contrast material has had time to occur. Comparison with the opposite side will show diminution of density when blood flow is decreased. The degree of occlusion which must be present to be detectable is yet to be determined.

It is recognized that excretory pyelograms may not reflect the true status of kidney function. Given enough time after injection, modern contrast media can be filtered through the glomeruli to visualize even a diseased kidney (13), though immediate pyelograms (one, three, and five minutes) may show relatively diminished excretion (Fig. 1, A). Early pyelograms are a less reliable and more indirect means of measuring renal blood flow; extrinsic factors affecting contractility of the collecting system, as well as variations in patient preparation, may be misleading. Absence of excretory function of a kidney with a normal collecting system as demonstrated by retrograde pyelography is also acceptable evidence of renal artery occlusion. Another exceptional instance occurs when the ischemic kidney puts out a small amount of concentrated urine with a denser

pyelogram than the contralateral side (11). The difference in concentration per unit volume could be due to differences in arterial or glomerular filtration pressure, or to pathologic changes brought about by exposure to severe hypertension of many years duration.

Conventional radiography and excretory pyelography may fail to demonstrate any abnormality in the presence of a renal artery lesion. Disparity of renal size or function was found in only half the cases in one series (10). Slight delay in appearance of contrast medium or 1 to 2 cm. difference in renal size was considered diagnostic. Howard called attention to the significance of a small kidney without evidence of atrophic pyelonephritis and emphasized the importance of complete evaluation of patients with the clinical syndrome despite normal intravenous pyelography (6).

Translumbar aortography is a more formidable procedure than intravenous aortography, and less adaptable as a screening method. Abnormalities of nephropacification during translumbar studies are not often reported. Laws, in discussing radiology in hypertension, states that a poor nephrogram may provide useful confirmatory evidence of diminished renal blood flow (7). The "comparative development of the nephrogram" is mentioned as a diagnostic point by Luke and Levitan (9). There are several reasons why differential nephropacification might not be apparent in a translumbar study. The customary test injection preloads the kidneys. A streaming effect may prevent equal amounts of contrast material from reaching each kidney. Similarly, if injection is distal to the renal arteries, retrograde flow during diastole may carry insufficient medium to the kidneys in unequal amounts.

Other screening procedures include differential renal function studies and radioactive iodine renography. Neither is without technical difficulty, and the former may be attended by complicating sequelae. The renogram reflects blood supply also, but is a less direct and more difficult

method. Its degree of reliability is considered less than that of the simplified radiographic method proposed.

SUMMARY

The efficacy of intravenous abdominal aortography as a screening test in appropriate cases of hypertension is discussed. A case report is presented to show differential nephropacity with unilateral renal ischemia. An intravenous bolus study with at least double the usual excretory urographic dose of iodide, followed by early pyelograms, is believed to be a safe and effective method of detecting occlusive renal artery lesions.

ACKNOWLEDGMENT: I am indebted to Dr. Henry S. Kaplan, Chairman, Department of Radiology, Stanford School of Medicine, for advice and assistance. Grateful acknowledgment is made to Dr. Grover J. Liese for the case illustrated in Figure 4, and to Dr. William H. Northway, Jr., for the case illustrated in Figure 5.

REFERENCES

1. DUSTAN, H. P., PAGE, I. H., AND POUTASSE, E. F.: Renal Hypertension. *New England J. Med.* 261: 647-653, Sept. 24, 1959.
2. EDLING, N. P. G., AND HELANDER, C. G.: Nephrographic Effect in Renal Angiography. An Experimental Study in Dogs. *Acta radiol.* 51: 17-24, January 1959.
3. EDLING, N. P. G., HELANDER, C. G., AND RENCK, L.: The Correlation Between Contrast Excretion and Arterial and Intrapelvic Pressures in Urography. An Experimental Study in Rabbits. *Acta radiol.* 42: 442-450, December 1954.
4. EVANS, J. A., DUBILIER, W., JR., AND MONTEITH, J. C.: Nephrotomography: A Preliminary Report. *Am. J. Roentgenol.* 71: 213-223, February 1954.
5. GREENSPAN, R. H., BERNSTEIN, E. F., AND LOKEN, M. K.: Intravenous Aortography: Technique and Clinical Aspects. *Am. J. Roentgenol.* 83: 1034-1041, June 1960.
6. HOWARD, J. E., BERTHRONG, M., GOULD, D. M., AND YENDT, E. R.: Hypertension Resulting from Unilateral Renal Vascular Disease and Its Relief by Nephrectomy. *Bull. Johns Hopkins Hosp.* 94: 51-85, February 1954.
7. LAWS, J. W.: Radiology in the Investigation and Management of Hypertension. *Postgrad. M. J.* 34: 514-523, October 1958.
8. LIESE, G. J.: Angiotomography: A Preliminary Report. *Radiology* 75: 272-274, August 1960.
9. LUKE, J. C., AND LEVITAN, B. A.: Revascularization of the Kidney in Hypertension Due to Renal Artery Stenosis. *Arch. Surg.* 79: 269-275, August 1959.
10. POUTASSE, E. F., AND DUSTAN, H. P.: Arteriosclerosis and Renal Hypertension; Indications for Aortography in Hypertensive Patients and Results of Surgical Treatment of Obstructive Lesions of Renal Artery. *J.A.M.A.* 165: 1521-1525, Nov. 23, 1957.
11. SCHLEGEL, J. U., SAVLOV, E. D., AND GABOR, F.: Some Studies in Renal Hypertension. *J. Urol.* 81: 581-595, May 1959.
12. VESEY, J., DOTTER, C. T., AND STEINBERG, I.: Nephrography: Simplified Technic. *Radiology* 55: 827-832, December 1950.
13. WINTER, C. C.: The Excretory Urogram as a Kidney Function Test. *J. Urol.* 83: 313-318, March 1960.

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SUMMARY IN INTERLINGUA

"Nephro-Opacification" Differential: Un Technica de Scrutinio pro Occlusion Unilateral de Arteria Renal

Le radiodensitate producite per sanguine cargate de substantia de contrasto e curante per le circulation renal, entrante simultaneemente in le filtrato glomerular e le cellulas tubular, es designate como "nephro-opacification." Es opiniate que le fidelitate de aortographia intravenose in le demonstration de iste opacification es superior a illo de aortographia translumbar e etiam a illo del renogramma a iodo radioactive.

Le technica optimal demanda leef-

fectuation simultanee de injectiones in le duo venas antecubital de 40 cm³ de substantia de contrasto de 85 pro cento, amontante a un dose total de 80 cm³. Isto es sequite immediateemente per le filmation. Roentgenogrammas serial es allora obtenite post un, tres, e septe minutas.

Es presentate un caso pro monstrar nephropacitate differential con ischemia renal unilateral. Es opiniate que le methodo es salve e efficace in le detection de lesiones occlusive del arteria renal.

Roentgen Diagnosis of Fibromuscular

Hyperplasia of the Renal Arteries¹

A. J. PALUBINSKAS, M.D., and EDWIN J. WYLIE, M.D.

FIBROMUSCULAR hyperplasia of the renal artery has recently been reported as a cause of renal arterial stenosis and secondary hypertension in a small number of cases. Leadbetter and Burkland (2) first described the entity in a five-and-one-half-year-old Negro boy. DeCamp and Birchall (1) reported a case in a twenty-three-year-old male. McCormack *et al.* (3) added 3 examples but did not mention the sex of their patients. Poutasse and Dustan (5) described "fibrous intimal proliferation" in the renal artery of 2 young persons with hypertension but they, also, failed to designate the sex. Wylie and Wellington (6) pointed out characteristic features of fibromuscular hyperplasia of the renal artery in 3 patients and made reference to an additional 5 cases.

The following report emphasizes the roentgen findings in 11 patients with fibromuscular hyperplasia of the renal arteries seen within a period of two years, including the cases described by Wylie and Wellington. Ten were investigated at the University of California Medical Center and 1 at the Veterans Administration Hospital, San Francisco, Calif.

The patients were all females between fifteen and forty-nine years of age, with hypertension known to have been present one week to twelve years. The blood pressure elevation was mild in 1 case and moderate to severe in the remainder, with a preoperative range of 170/100 to 250/140. In 3 patients the hypertension was asymptomatic. All but 1 had an audible systolic bruit in the upper abdomen.

To date 9 of the patients have been explored surgically. In each, the stenotic lesion in the renal artery or arteries was found to be due to hypertrophy of the muscular elements and, to a lesser extent, to the fibrous connective-tissue ele-

ments of the media of the vessels. Arterial reconstructive procedures were performed in all cases with the exception of 1 in which nephrectomy was done. Following operation, blood pressure returned to normal levels in 5 and decreased significantly, but not to normotensive levels, in 3 patients. Hypertension returned in 1 instance after an initial postoperative decrease in blood pressures; renal arteriography demonstrated development of further arterial stenosis.

ROENTGEN FEATURES

Location: Unlike arteriosclerotic narrowings of the renal arteries, which tend to occur predominantly within the medial third of the vessel, fibromuscular hyperplasia appears to involve primarily the middle and/or distal third and may extend into the proximal branches of the main renal artery. In the present series the right renal artery alone was involved in 7 patients, both arteries in 3, and the left artery in 1.

Appearance: In each instance the area of involvement presented a distinctive appearance on renal arteriography. The most common configuration is best described as a contrast-outlined image resembling a string of beads of varying size (Fig. 1, A and B). With shorter or greater lengths of vessel between the sharply constricted areas a corrugated or accordion-pleated appearance (Fig. 1, C and D, Fig. 2, A and B) was assumed or one resembling a string of short sausages (Fig. 1, A and B). The other major pattern noted was roughly similar to the napkin-ring deformity seen in constricting bowel neoplasms.

Poststenotic dilatation of the renal artery or of its main branches was evident in some instances (Fig. 2, C and D), with

¹ From the Departments of Radiology and Surgery, University of California School of Medicine, San Francisco, Calif. Accepted for publication in August 1960.

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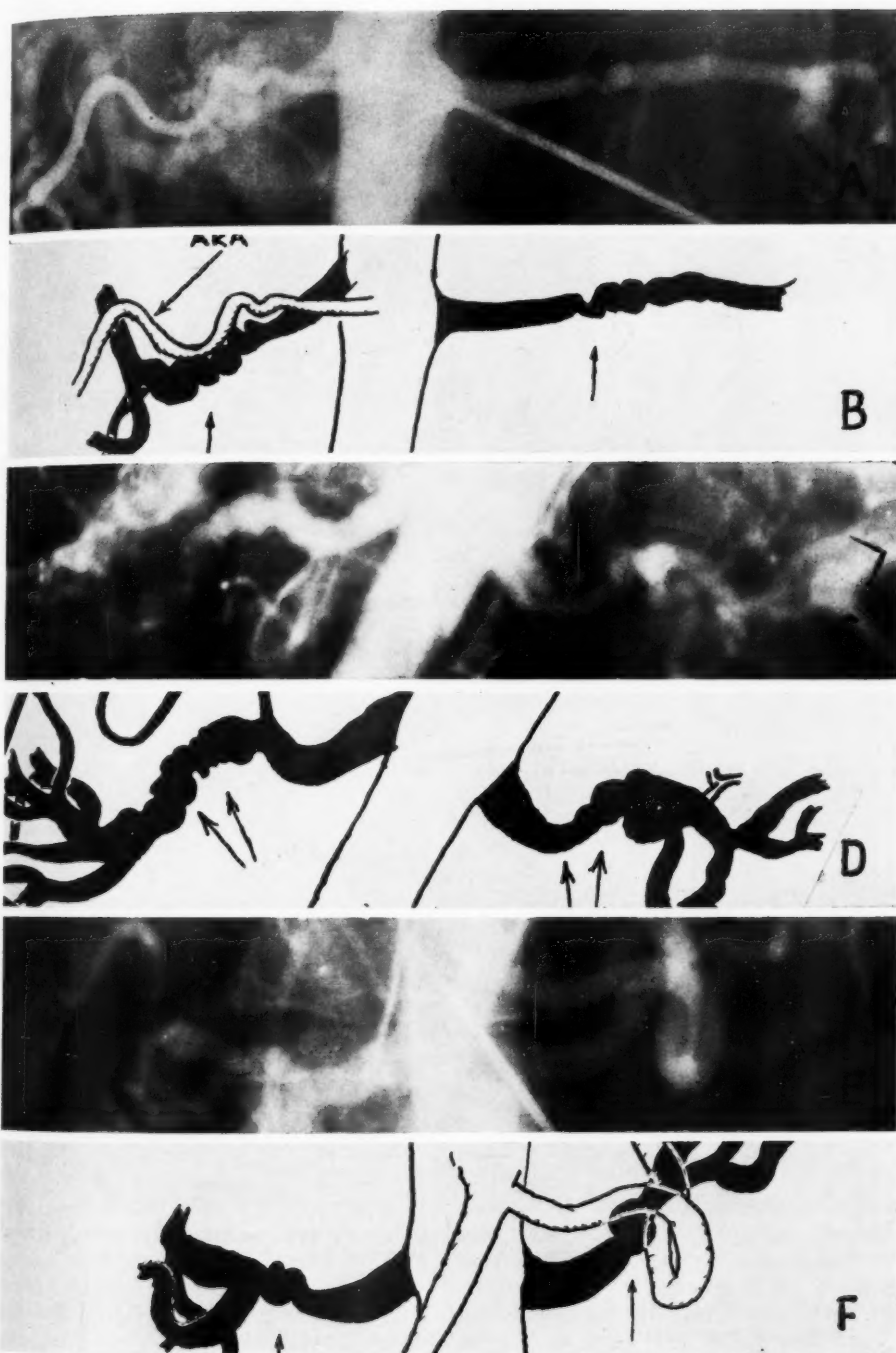


Fig. 1. Bilateral renal artery fibromuscular hyperplasia in 3 patients. The renal arteries are blacked in on the corresponding pen-and-ink sketches of the renal arteriograms. Arrows direct attention to the involved areas. ARA indicates an accessory renal artery.

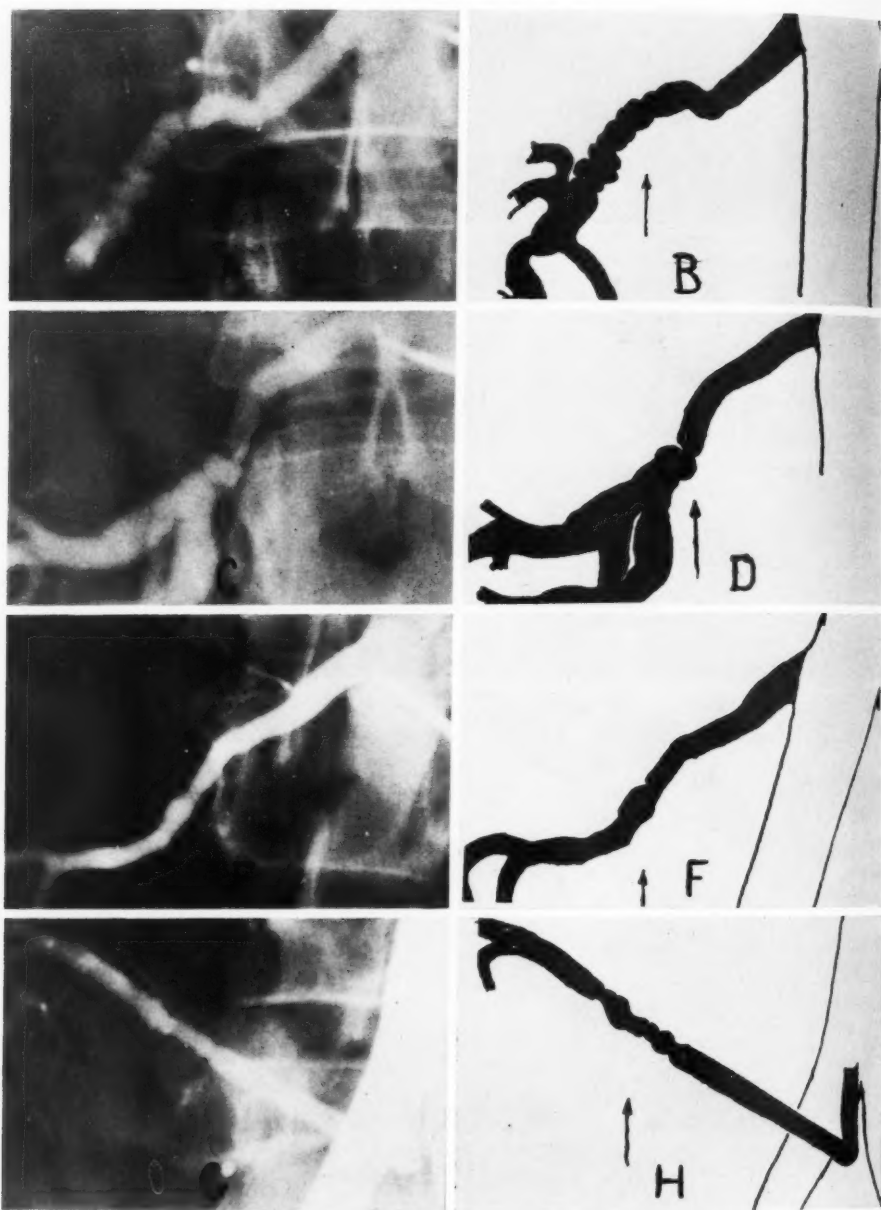


Fig. 2. Unilateral right-sided fibromuscular hyperplasia. G and H show the renal artery arising from the proximal portion of the right common iliac artery.

berry-aneurysm formation within the area of fibromuscular hyperplasia in at least 2 cases (Fig. 3, C and D). Pathologic study showed these aneurysms to be the

result of localized defects in the otherwise hypertrophied media.

Kidney Size: The right kidney on plain films of the abdomen ordinarily appears

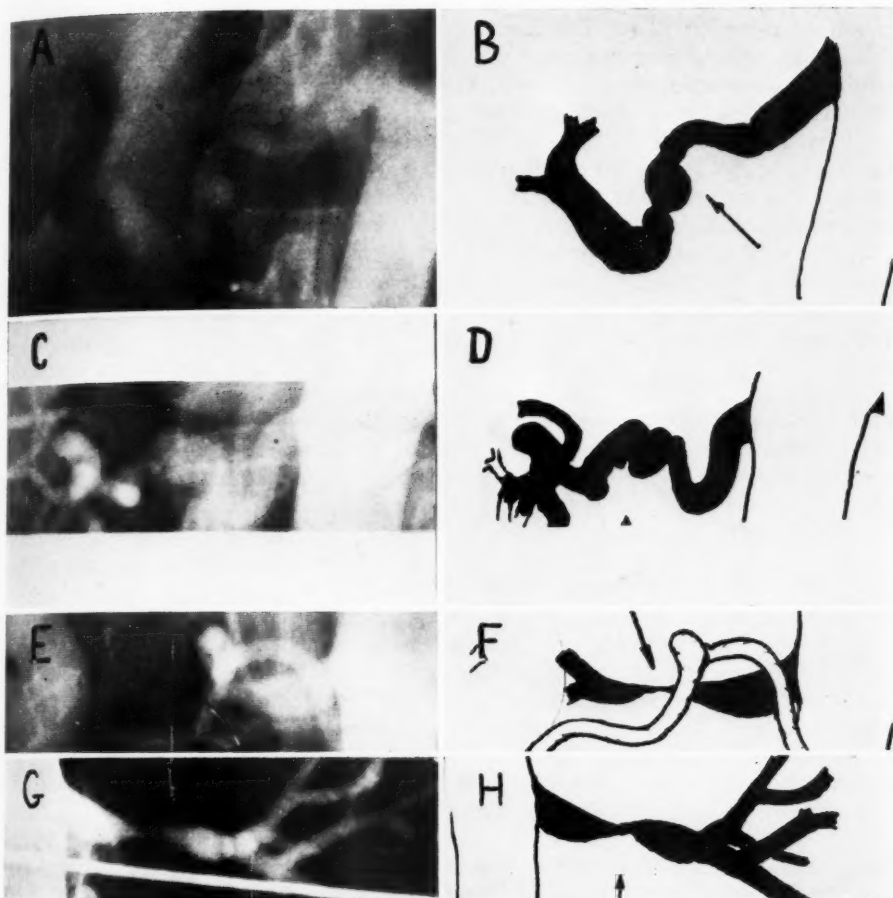


Fig. 3. Unilateral fibromuscular hyperplasia of the renal artery, left-sided in one instance. In E and F the vessel overlying the narrow portion of the right renal artery is an accessory renal artery. The portion of the renal artery distal to this narrowing is poorly demonstrated on the single roentgenogram; the pen-and-ink sketch represents a composite of several films of a series.

slightly smaller and a little shorter than the left (4). In the present series, in those patients with unilateral renal disease, a significant reduction, not only in the long diameter (the most convenient measurement) but also in the overall size of the kidney on the involved side was apparent. Reduction in kidney length varied from 0.5 to 6.5 cm., with a mean of 2.4 cm. Where bilateral renal artery involvement was present, the kidney appeared significantly smaller on the side with the most prominent involvement of the renal artery, except in 1 patient. In that in-

stance, however, an undiseased accessory artery also supplied the kidney whose main artery showed the most prominent fibromuscular hyperplasia.

Promptness of Appearance and Density of Contrast Medium: Slightly delayed excretion and lesser density of the contrast medium excreted by the kidney on the involved side were apparent in several of the patients, but in the remainder there were no obvious differences. In 1 patient a marked decrease was shown in the density of the nephrogram on the involved side, on films obtained promptly after rapid

intravenous injection of the contrast material. Such roentgenograms may prove helpful in evaluation of the relative "function" of the two kidneys. Postoperatively, several patients showed increased density of excretion of the kidney on the operated in comparison with the normal side.

The results of divided function studies (J. E. Howard study) were helpful in demonstrating decreased function of the involved kidney in some cases, but frequently were inconclusive.

DISCUSSION

Fibromuscular hyperplasia of the renal arteries appears to be the cause of previously unexplained hypertension in a significant number of young females, as judged by the number of cases in this series, all seen within a period of two years. Exclusive of the report of Wylie and Wellington, the sex of only 2 patients is stated in the literature (1, 2). Both were males. It appears significant that all patients in the present series were females.

The etiology of the lesion is unknown. No evidence of endocrinopathy was encountered in the present group. Some authors have considered the lesion as congenital in origin (1, 2).

Some findings suggest that the hyperplasia may be secondary to chronic stretching of the renal artery in patients with kidneys that are more mobile than usual. Generally, motility of the kidneys in the female tends to be somewhat greater than in the male. This may explain the decided sex affinity demonstrated in this series. Pregnancy would represent an added element of chronic stretching and tension of the renal artery. Further study is in progress to determine whether the length of the artery and factors producing chronic recurrent tension of the vessel are of etiologic importance in the development of fibromuscular hyperplasia.

Early surgical reconstruction of the involved renal arteries appears to be the treatment of choice. Nephrectomy may sometimes be necessary. Further investigations will, no doubt, indicate

whether some type of nephropexy need be done at the same time.

Excretory urograms can provide useful information regarding size, position, and mobility of the kidneys, and promptness and density of excretion. Renal arteriography is the definitive diagnostic examination. The distinctive configurations of lesions noted in the present series have led to such descriptive terms as "accordion-pleating" and "string-of-beads" sign.

Several technics for roentgen visualization of the renal arteries are currently in general use. Satisfactory renal arteriograms have been obtained at the University of California Medical Center by direct injection of contrast medium into the aorta near the level of the renal arteries, either through a translumbar needle or through a catheter passed up into the aorta through one of the common femoral arteries. Some investigators favor the intravenous technic, with serial exposures after the rapid injection of contrast medium, usually into one or both antecubital veins.

The differential diagnosis should include consideration of those processes which could be responsible for narrowing of the lumen of the renal artery. Although arteriosclerotic narrowing does occur beyond the proximal third of the renal artery, it is most often encountered at the origin or within the proximal third of the vessel, generally in older patients with demonstrable arteriosclerotic disease of the adjacent aorta and major pelvic arteries. Arteriosclerotic plaques in the vessels sometimes have more jagged, irregular margins.

Focal overlap of a tortuous renal artery could cause some indecision in diagnosis, especially in examinations where the artery is not sharply outlined by contrast medium. This has not been a problem up to the present time, but if such indecision exists, stereoscopic or oblique studies could be of assistance.

The renal artery of the hypoplastic or atrophic kidney is generally reduced in caliber, but this reduction is symmetrical throughout, without focal stenoses, aneurysms, or poststenotic dilatations.

Ancillary historical or clinical findings should serve to distinguish the uncommon instances of narrowing of the renal arteries due to trauma or neoplasm.

SUMMARY

The roentgen appearance of fibromuscular hyperplasia of the renal artery or arteries producing arterial stenosis and secondary hypertension is described on the basis of 11 cases, all in females. Criteria for the diagnosis of this recently recognized arterial lesion are presented. It should be suspected in unexplained hypertension, especially in a female below the age of fifty. Careful auscultation for upper abdominal bruits should be made. Excretory urography provides valuable information, but renal arteriography is the definitive diagnostic study.

ADDENDUM: We have now seen renal artery stenoses caused by fibromuscular hyperplasia in 18 hypertensive patients; 17 of these were females, and 1 was an eleven-month-old white male infant. Thirteen patients, including the male infant, have

been operated upon and the lesion has been verified microscopically.

One of the patients undergoing operation had a combined lesion, atherosclerotic narrowing of the proximal renal artery and fibromuscular hyperplasia of the more distal portion of the artery. Such combined lesions have now been demonstrated by arteriography in 3 patients, all older adult females.

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REFERENCES

1. DeCAMP, P. T., AND BIRCHALL, R.: Recognition and Treatment of Renal Arterial Stenosis Associated with Hypertension. *Surgery* **43**: 134-151, January 1958.
2. LEADBETTER, W. F., AND BURKLAND, C. E.: Hypertension in Unilateral Renal Disease. *J. Urol.* **39**: 611-626, May 1938.
3. McCORMACK, L. J., HAZARD, J. B., AND POUTASSE, E. F.: Obstructive Lesions of the Renal Artery Associated with Remediable Hypertension. *Am. J. Path.* **34**: 582, May-June 1958.
4. MOELL, H.: Size of Normal Kidneys. *Acta radiol.* **46**: 640-645, November 1956.
5. POUTASSE, E. F., AND DUSTAN, H. P.: Arteriosclerosis and Renal Hypertension; Indications for Aortography in Hypertensive Patients and Results of Surgical Treatment of Obstructive Lesions of Renal Artery. *J.A.M.A.* **165**: 1521-1525, Nov. 23, 1957.
6. WYLIE, E. J., AND WELLINGTON, J. S.: Hypertension Caused by Fibromuscular Hyperplasia of the Renal Arteries. *Am. J. Surg.* **100**: 183-193, August 1960.

SUMMARIO IN INTERLINGUA

Diagnose Roentgenologic de Hyperplasia Fibromuscular del Arterias Renal

Hyperplasia fibromuscular del arteria renal, producente stenosis del arteria con hypertension secundari, es reportate in 11 patientes, omnes feminin, de etates de inter dece-cinque e quaranta-novem annos. Operationes de reconstruction arterial esseva effectuate in octo del casos e nephrectomia in un, con le resultado de un reduction del tension de sanguine.

Urographia excretori provide utile information in iste condition, sed arteriographia renal es le definitive modo de

studio diagnostic. Le aspecto roentgenologic le plus commun es illo de un filo de perlas de varie dimensiones. In le presentia de plus curte o plus longe distantias de vaso inter le acutemente constringite areas, un apparentia corrugate, etiam un apparentia de accordion, se manifesta, o un de resimilantia con un guirlanda de curte salsicias. Le altere major configuration esseva grossiermente simile al deformitate de "anulo de servietta" in casos de constriction intestinal per neoplasma.

A New Packing and Spacing Material for Use in Carcinoma of the Cervix Uteri

Preliminary Report¹

J. C. WEISMAN, M.D.

EVER SINCE radioactive sources have been in use for the local treatment of carcinoma of the cervix uteri, it has been customary to use one-inch gauze packing to retain the sources in position and to hold them at a maximum distance from the mucosa of the urinary bladder and rectum. If such spacing is to be adequate, the gauze must be firmly packed against sensitive and often bleeding or eroded mucosa. Removal of the packing after seventy-two to ninety-six hours is associated with extreme pain and bleeding. Erosion is produced by pressure, with resultant infection. The odor due to retained secretions is offensive to the patient as well as to attending personnel. No matter how expertly it is placed, the moist gauze contracts, with a reduction of the estimated spacing and often a change in the position of the radium applicator. This results in uneven distribution of radiation and the production of unwanted hot spots.

After a number of inquiries for a gauze substitute, the writer was directed to the O-Cel-O Corporation² which makes a polyurethane foam material which seems to be ideal for the above purpose. This is a polymer of high molecular weight, made by the reaction of tolylene diisocyanate to a polyester resin (polydiethylene adipate) in the presence of water, catalyst (N-methyl morpholine), tricresyl phosphate, and emulsifier. The material is apparently neutral chemically. It has a flesh-soft texture and is resilient and absorptive, with a tendency to retain its original shape after compression in the dry or moist state. It is inert to most solvents, such as alcohol, ether, and ben-

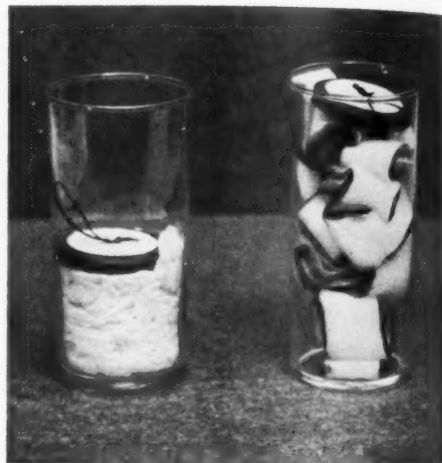


Fig. 1. Illustrating the resilient property of the foam strip packing. The glass on the left contains 5 yards of 1-inch gauze packing compressed by a small lead wafer weighing a few ounces. That on the right holds 1½ yards of foam strip packing compressed by a similar lead weight. The edges of the foam packing have been tinted for better clarity.

zene, but is subject to either alkaline or acid hydrolysis.

Strips of this material 1 inch in width and 1/4 inch in thickness were kindly furnished by the manufacturer for this study. When these foam strips were packed in glass jars and autoclaved, the original properties were well preserved, although, after being autoclaved more than once or twice, they suffered some loss of resiliency and underwent a change in color to a light brown. Figure 1 illustrates the resilient property of the foam strip packing. The glass on the left contains 5 yards of 1-inch gauze packing compressed by a small lead wafer weighing a few ounces; that on the right contains 1 1/2 yards of foam strip packing com-

¹ From the Department of Radiology, Florida Sanitarium and Hospital, Orlando, Fla. Accepted for publication in September 1960.

² O-Cel-O Department, General Mills, Inc., Tonawanda, N. Y.

pressed by a similar lead weight. The edges of the foam packing have been tinted for better clarity. Note its obvious advantages for spacing.

The packing is carried out by conventional methods; the vagina is ballooned out readily for insertion of the foam strip with a long forceps. Removal seventy-two or ninety-six hours later is simple. The strip of packing bulges and is easily picked up. The patient is agreeably surprised at the lack of pain. There is less odor and discharge, since the foam permits interstices for drainage.

The manufacturers plan to attempt incorporation of an opaque thread in the strips so that x-ray examination for position of the applicator will also give a picture of the distance of the source to the mucosa of the urinary bladder and rectum. This could be measured directly on the film.

Textbooks on radiation therapy have

little to say as to methods and materials for packing a radium applicator. The importance of adequate spacing has not been stressed, and no mention was found in available books, of a method of actually measuring the space, though most texts do mention the necessity of a follow-up radiograph of the pelvis to check the position of the applicator.

Further work is contemplated to obtain measurements with the opaque-threaded packing. It is hoped that by the use of this visual method some of the unfortunate sequelae of vesicovaginal and rectovaginal fistulae as well as irreversible cystitis and proctitis can be avoided.

NOTE: The author wishes to acknowledge the cooperation of Mr. Albert F. Reilly, Research Director, General Mills, Inc., O-Cel-O Department.

The photograph is reproduced by the courtesy of Benjamin Glaser, M. D.

Department of Radiology
Florida Sanitarium and Hospital
Orlando, Fla.

SUMMARIO IN INTERLINGUA

Un Nove Material de Paccation e de Spatiation pro le Uso in Carcinoma del Cervice

Certe disadvantages es associate con le uso de gaza como material de paccage pro mantener le position interne del fontes de radioactivitate usate in le tractamento de carcinoma del cervice e pro ager como spatiantes in le mantenentia de un adequate distantia inter tal fontes e le mucosa

del vesica e del recto. Le autor ha usate un material spumose de polyurethano que es fabricate per le Corporation O-Cel-O. Iste material es molle e resiliente. Le insertion de illo es facile. Illo pote esser extrahite sin difficultate. Le disconforto pro le patiente es minimal.



Preparation of the Colon with a New Senna Compound¹

CHARLES W. REAVIS, M.D., THOMAS S. LONG, M.D., WILLIS E. LEMON, M.D.,
and LAWRENCE R. NICKELL, M.D.

EMPTYING OF the colon is necessary for the proper conduct of many radiographic examinations of abdominal organs. This paper reports our experience with a new senna preparation, Roenten,² as a colon evacuant. The study was conducted to compare the patient acceptance, associated discomfort, and cleansing efficiency of this compound and castor oil.

The active ingredient of Roenten is 2,000 mg. of the dried leaflets of *Cassia angustifolia* (senna) biologically assayed (1, 2). Our previous experience with a

powdered form, chocolate-flavored, in a single dose container and is administered as a suspension in one-half to three-quarters of a glass of water. The cost of a single dose of Roenten is roughly twice that of 2 ounces of castor oil. The usual contraindications for catharsis are also contraindications for Roenten.

A total of 385 adult patients were included in our combined series, 219 receiving Roenten and 166 receiving 2 ounces of castor oil. All patients were hospitalized, thus permitting control of

TABLE I: COMPARATIVE EFFICIENCY OF ROENTEN AND CASTOR OIL FOR BOWEL CLEANSING PRIOR TO ROENTGENOGRAPHY

	Barium Enema		Cholecystogram		Intravenous Pyelography with Enemas		Intravenous Pyelography Without Enemas		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%
Roenten										
Satisfactory	48	73.8	78	88.6	17	85	41	89.1	184	84
Poor	17	26.2	10	11.4	3	15	5	10.9	35	16
TOTAL	65	100	88	100	20	100	46	100	219	100
Castor Oil										
Satisfactory	47	65.3	14	60.9	37	72.5	15	75	113	68.1
Poor	25	34.7	9	39.1	14	27.5	5	25	53	31.9
TOTAL	72	100	23	100	51	100	20	100	166	100

1,600-mg. preparation proved this smaller dosage to be inadequate. Podophyllum (mandrake root), Asarum (Canada snake root), fennel seed, and Glycyrrhiza (licorice root) are included in the preparation, supposedly to reduce the amount and severity of cramping.

Senna anthracene compounds are thought to be absorbed in the small bowel, ultimately reaching the colon by the blood stream and stimulating colonic contraction, presumably through Auerbach's plexus (3). Stools induced tend to be formed rather than watery. The laxative is available in

their preparation. The laxatives were given three hours following a clear-liquid supper. If a barium-enema was to be given, the patient received cleansing enemas in the morning prior to the procedure. For the purpose of this study all patients undergoing oral cholecystography received cleansing enemas as well as the indicated laxative. Many of the patients undergoing intravenous pyelography were also given cleansing enemas, usually because the procedure was combined with a barium-enema study or cholecystography.

On arrival of the patient in the radiology

¹ From the Department of Radiology, Baroness Erlanger Hospital, Chattanooga, Tenn. Accepted for publication in September 1960.

² Roenten used in this study supplied by Brayten Pharmaceutical Co., Chattanooga, Tenn.

department the technician recorded the preparation used and the presence or absence of abdominal discomfort. As each set of films was interpreted, the radiologist made a record of the efficiency of bowel cleansing as satisfactory or poor. Four radiologists and three residents recorded their impressions for their individual examinations. Results of the study are presented in Table I.

It is noted that the percentage of unsatisfactory cleansing with Roenten is lower than with castor oil. The senna preparation, with its chocolate flavor, is more palatable and thus more easily accepted by the patient. The presence of cramping was noted by 19 per cent of those receiving Roenten and by 20 per cent of those receiving castor oil.

CONCLUSIONS

1. Roenten is as effective as castor oil as a bowel cleansing agent for radiography.
2. No significant difference in the occurrence of abdominal cramping was noted in a comparison of the two evacuants.
3. The senna preparation is more palatable.

Baroness Erlanger Hospital
Chattanooga, Tenn.

REFERENCES

1. GROTE, I. W., AND WOODS, M.: Laxative Action in Mice of Tinnevely and Alexandria Senna, and of Several Botanically Related Plants. *J. Am. Pharm. A. (Sc. Ed.)* **33**: 266-270, August 1944.
2. GROTE, I. W., AND WOODS, M.: Laxative Activity in Mice of the Various Parts of the Senna Plant. *J. Am. Pharm. A. (Sc. Ed.)* **40**: 52-53, January 1951.
3. DRILL, V. A.: *Pharmacology in Medicine*. New York, The Blakiston Division of McGraw-Hill Book Co., 2d ed., 1958, pp. 675, 677.

SUMMARIO IN INTERLINGUA

Preparation del Colon con un Nove Composito de Senna

Esseva facite un studio comparative de Roenten (un preparato de senna) e oleo de ricino usate como evacuantes colonic ante le roentgenographia abdominal. Roenten esseva administrate in un dosage de 2.000 mg a 219 patientes, oleo de ricino in un

dosage de 2 uncias a 166. Le duo agentes esseva equalmente efficace como agentes de purgation. Le incidentia de crampos abdominal non differeva significativamente. Roenten esseva plus palatabile e assi acceptate plus prestemente.

EDITORIAL

On the Labeling of Shadows

For one word a man is often set down as wise, and for one word he is as often set down as a fool.— CONFUCIUS

Radiology is a relatively fast moving discipline. Its routines—including the preparation of roentgen reports—must therefore be reappraised at periodic intervals. Such reappraisal ought to start with a retrograde review of the procedure under consideration. Dialectic analysis of the essentials thus uncovered is educational and otherwise rewarding. It should go as far back as bare truisms, since re-emphasis placed on some antique tenet—so self-evident as to be disguised in, and disregarded as, a platitude—may give the old routine a new lease on life.

Referring specialists often wish to make their own interpretations, a privilege which must never be challenged. Knowing more about the particular patient, and perhaps more about the roentgen minutiae of the area under considerations, they seem to get more out of (or read more into) the films. A few of these gentlemen, on the other hand, discard the roentgen reports without so much as glancing at them, which again is their privilege. As a result, though contrary to the graphorrhea of private roentgen practice, in some highly regarded teaching institutions, roentgen reports for certain departments (orthopedics, urology, and the like) are issued in a sloppy, bureaucratic manner—just to have something on paper. While nobody is perfect, by comparison with a roentgenologist the orthopedist is more likely to miss gallstones, the urologist more prone to overlook osteolytic lesions, the internist more apt to ignore prostatic calcifications.

But when these neglected shadows finally come to the fore, the old roentgen report is checked, and it is then better to have *all* its shadows labeled, correctly if possible. Under existing circumstances, it is not as incongruous as it seems to remind the radiologic fraternity that reporting is the most essential of its diagnostic tasks.

At first glance, a fluoroscopic examination is less glamorous than Hamlet's sarcastic tirade, aimed at his queen-mother:

*Come, come, and sit you down; you shall not budge;
You go not till I set you up a glass
Where you can see the inmost part of you.¹*

A roentgen ritual is also less dramatic than the lonely Dane's vindictive misdeemeanors. And yet, on the simple strength of its prognostic implications, a roentgen examination is just as much a matter of life and death. Besides, it leaves at least two mementos, the technician's roentgenogram (or set of roentgenograms) and the roentgenologist's report.

In their private offices, many roentgenologists will retain only a very few roentgenograms, selected from unusual cases. Most films are either sent to the referring physicians or are discarded, albeit not immediately. Dr. Eugene Lutterbeck justifies this procedure by referring to clinical laboratories, which do not preserve

¹ Silvanus Phillips Thompson (1851-1916) "discovered" this quotation (Act 3, Scene 4), and regarded it almost as a Shakespearean premonition of fluoroscopy (1). The triplet has fascinated many others (2-5). Thus the historian of radiology, Dr. Isadore Trostler (1869-1957), asked at least twice (6, 7) what (other than the proverbial crystal ball) it meant.

samples of blood or urine, even if this were practicable.² Conversely, in private offices, copies of the roentgen reports are invariably kept for decades—"indefinitely" if sufficient storage space is available.

In large hospitals and clinics, all (except the current and the teaching) films are eventually destroyed (8), at times only after some of them have been "filed" (9) in the guise of miniaturized substitutes. In the Department of Radiology of Cook County Hospital (Chicago), since 1957 (shortly after Irvin Franklin Hummon, Jr., became director of the department) all roentgenograms are copied on microfilm (as a last step in processing, after sorting but before the reporting). With the volume on hand, this exceeds one million frames (*one mega-frame*) every two years. It poses in itself a serious storage problem, if single frames are to remain available for reference. The original roentgen reports, attached to the hospital records, are stored for a longer time. Furthermore, hospital records are also microfilmed, page by page, and microfilms of hospital records are preserved much longer than microfilms of roentgenograms.

Roentgen reports prepared before 1920 are scarcer than incunabula, but the *average* roentgen report of today survives just a little longer than all the other vestiges of a given roentgen examination.

Indeed, it takes only a few weeks and the alibis, excuses, and related incidents—from (a) the processing solutions which were too hot or too cold, (b) the films fogged in transit, and (c) the patient's inadequate preparation and/or lack of co-operation, to (d) the hasty viewing blamed on lack of time due to lengthy personal consultations, (e) the defective dictating device and/or the inattentive secretary, and (f) the fleeting wet-film remarks not incorporated in the report—are all forgotten. At that stage of procedural amnesia, retrospective judgment of roentgenologic valor rests on pure, unmitigated documentary

evidence, *i.e.*, on the roentgen report.

Considering the obvious (and even more so the latent) significance of proper reporting for an adequate practice of roentgenology, one wonders why is it that so little importance has been attached to this phase in the graduate teaching of radiology? Perhaps one of the February teaching sessions of the American College of Radiology should be devoted to this problem.

An early expert in forensic radiology, and founder of the American College of Radiology, Dr. Albert Soiland (1873-1946), contended in 1918 that, if requested by court, he must furnish either "a print, a copy, or a written report" (10). This has been borne out by subsequent developments. In the opinion of one of today's authorities on such matters—the Ann Arbor roentgenologist, Dr. Samuel Wright Donaldson—microfilms are admissible in court, at least as secondary or best evidence (11). In actual instances, though, when films were no longer available, the courts have accepted instead the sole opinion—that is to say *the report*—of the roentgenologist (12).

When it is subpoenaed in court (13), or before the discriminating audience of a surgical conference, or summoned by the clinico-pathologic tribunal of last resort, or simply by the attending physician for a quizzical retrospective glance, the (carbon copy of the) roentgen report must be both crisp and stalwart: it faces ever-present wordmongers, always ready, willing, and able to indulge in lingual dissection.

At that decisive moment, be the report concocted in a few, *swept* terms, or *garnished* with many uncouth vocables, if it should fail to come up with an adequate answer, it remains but *empty* prose, that is, what the Kit-Kat (14) physician-poet, Sir Samuel Garth (1661-1719), would have called "a barren superfluity of words!" Whereas, if the words had been offered by weight, not by number, nor with haste, and if they had solved the points in question, those particular shadows were correctly labeled.

² Personal communication.

and would never come back to haunt the roentgenologist.

E. R. N. GRIGG, M.D.

REFERENCES

1. THOMPSON, S. P.: Presidential Address, British Roentgen Society. *Arch. Roentgen Ray* **2**: 23-30, Nov. 5, 1897.
2. KAYE, G. W. C.: *Roentgenology*. New York, Paul B. Hoeber, 1928, p. 1.
3. KELLS, C. E.: *Three Score Years and Nine*. New Orleans, Privately Printed, 1926, p. 398.
4. GARLAND, L. H.: Scientific Importance of X-Rays. *Elec. Engineering* **64**: 978-988, December 1945.
5. LEWALD, L. T.: X-Ray Discovery Excites New York. *Academy Bookman* **5** (3): 1-13, Fall 1952.
6. TROSTLER, I. S.: The Original Communication of the Discovery of the Roentgen Rays. *Am. J. Phys. Therapy* **7**: 95-99, June 1930.
7. TROSTLER, I. S.: Some Interesting Highlights in the History of Roentgenology. *Am. J. Phys. Therapy* **7**: 447-456, February 1931.
8. CARMAN, R. D.: The Making and Filing of Records in the Section on Roentgenology in the Mayo Clinic. *Am. J. Roentgenol.* **8**: 372-382, July 1921.
9. SUTHERLAND, C. G.: A Proposed New Method: the Filing of Roentgenograms. *Hospitals* **15**: 173-175, March 1918.
10. SOILAND, A.: The Medico-Legal Status of the Roentgenologist. *Am. J. Roentgenol.* **5**: 173-175, April 1918.
11. DONALDSON, S. W.: *The Roentgenologist in Court*. Springfield, Ill., Charles C Thomas, 2d Ed., 1954, p. 215.
12. TROSTLER, I. S.: The Legal Aspects of Identification and Interpretation of Roentgenograms. *Am. J. Roentgenol.* **32**: 680-693, November 1934.
13. Legal Status of Hospital Records. *Editorial Radiology* **14**: 520-521, May 1930.
14. CUSHING, H.: Dr. Samuel Garth, the Kit-Kat Poet. *Bull. Johns Hopkins Hosp.* **17**: 1-7, January 1906.



IN MEMORIAM



SAMUEL BROWN, M.D.

1886-1960

In the death of Dr. Samuel Brown of Cincinnati, on Dec. 5, 1960, the medical profession has lost a most distinguished member, and the community a beloved citizen.

Samuel Brown was born in Russia in 1886 and came to America as a young man of nineteen. He worked his way through the University of Tennessee Medical School, graduating in 1911. While serving his internship in the Copper Queen Hospital (Bisbee, Ariz.), he became interested in the field of cancer therapy, and went on, as a resident, to the Memorial Hospital for Treatment of Cancer and Allied

Diseases in New York. He served there from 1912 to 1917, working principally with radium, coming in contact at that time with many pioneers in the field, including Dr. Henry H. Janeway and Dr. James Ewing.

During World War I, Dr. Brown served from 1917 to 1919 as a major in charge of the x-ray laboratory at Camp Sherman, in Chillicothe, Ohio. While there he worked with many doctors from Cincinnati, including Drs. Christian Holmes, Roger Morris, Alfred Friedlander, and Moses Salzer, who influenced him to establish a private practice in

that city following his discharge from the Armed Forces. Shortly thereafter, in 1921, he was married to Bernice Stern, who became his devoted and lifelong helpmate and now survives him.

In 1922 Dr. Brown became associated with the Jewish Hospital in Cincinnati, where he assisted in the founding of the Department of Radiology. Under his guidance, the Department flourished and rapidly became a most important focal point of medical interest within the hospital, even in those days when x-rays were used much less extensively than at present. Samuel Brown was a pioneer in many ways and, with his vivid imagination and original thinking, he came up with many new ideas for both diagnostic and therapeutic application of x-rays. He organized the first private hospital residency in radiology in Cincinnati, a program which has been continued and expanded greatly up to the present time. He served as director of the Jewish Hospital Department of Radiology until 1950, after which he continued in private practice until recently, when declining health forced him into retirement.

Samuel Brown was a prolific writer, having made more than sixty contributions to the scientific literature. Much of his earlier work had to do with the diagnosis of abdominal tumors and with emphasis on the lateral views of the chest and gastrointestinal tract. He presented many exhibits at meetings of various societies, particularly the Radiological Society of North America. In 1931, he received an award for the excellence of an exhibit on "Interlobar Effusions." Also, for several years he conducted refresher courses at the meetings of the Radiological Society of North America on the subjects of "Abdominal Tumors" and "Biliary Tract Lesions." In addition to his affiliation with that organization, Dr. Brown was a member of the Cincinnati Academy of Medicine, the American Medical Association, and of the World Medical Association; he was a Fellow of the American College of Radiology and an assistant professor of Radiology at the University of Cincinnati College

of Medicine. He was one of the earliest diplomates of the American Board of Radiology (1934).

Intensive and painstaking hard work characterized all of Samuel Brown's life. He had struggled and worked hard as a young man going through school. He never cultivated any hobbies in the usual sense, for his work was his diversion as well as his vocation. He accumulated an enormous collection of teaching slides over the years, having prepared every one of them himself to meet his exacting standards. In his early days at the Jewish Hospital he had very little help and he did most of the technical work himself, as well as the interpretation of the examinations. All of this he accomplished with boundless enthusiasm and energy. He would literally run from the film-taking room to the dark room and process the films himself, so eager was he to learn the outcome of an examination. This habit of hard personal work was carried over into later years even when he had ample technical and professional assistance at his command. He was utterly fascinated by unusual cases and would go to a great deal of trouble to persuade a difficult patient with an interesting problem to be examined in the x-ray laboratory. This sort of interest was accompanied by a readiness to teach and explain problems, which will always be fondly and gratefully remembered by those who worked with him. His tremendous enthusiasm in the preparation of exhibits, papers, and lectures was most contagious and stimulated his colleagues to put forth their best efforts in similar endeavors.

A very warm-hearted person, he was always most generous in his contributions to various philanthropies, and he played a role as an active worker in a number of charitable and educational causes.

All of the associates, residents, technicians, and others who served with Dr. Brown felt a great affection for him and experienced a deep sense of personal loss on the occasion of his passing. As a physician, radiologist, human being, and friend, he will be greatly missed.

LEE S. ROSENBERG, M.D.

ARCHIE FINE, M.D.

ANNOUNCEMENTS AND BOOK REVIEWS

SEVENTH INTER-AMERICAN CONGRESS OF RADIOLOGY

The Seventh Inter-American Congress of Radiology will be held in São Paulo, Brazil, Sept. 3-10, 1961. Delegates from the United States, appointed by the American College of Radiology, the American Roentgen Ray Society, the Radiological Society of North America, the American Radium Society, and the Section of Radiology of the American Medical Association, are: Eugene P. Pendergrass, M.D., Philadelphia, Penna., Chairman; Thomas Bond, M.D., Fort Worth, Texas; Lois C. Collins, M.D., Houston, Texas; J. A. del Regato, M.D., Colorado Springs, Colo.; Philip J. Hodes, M.D., Philadelphia, Penna.; Jesshill Love, M.D., Santa Barbara, Calif.; Wendell G. Scott, M.D., St. Louis, Mo.

During the Congress, The American College of Radiology will hold a special convocation to bestow Honorary Membership on three Latin-American radiologists.

Requests for registration blanks and hotel reservation forms should be addressed to the Secretary of the Congress, Dr. Walter Bomfim-Pontes, Rua Marconi 94, São Paulo. The Lee Kirkland Travel Agency, 1231 Baltimore Ave., Kansas City, Mo., is organizing special charter tours of interest to radiologists.

GREATER MIAMI RADIOLOGICAL SOCIETY

Recently elected officers of the Greater Miami Radiological Society include: President, George P. Daurelle, M.D.; Vice-President, Donald H. Altman, M.D.; Secretary-Treasurer, Carl E. Balli, M.D., 907-8 Huntington Medical Building, Miami 32, Fla.

The meetings will continue to be held the third Wednesday of each month, at 8:00 P.M., at Jackson Memorial Hospital, Miami.

KANSAS RADIOLOGICAL SOCIETY

At the annual meeting of the Kansas Radiological Society held Feb. 20, 1961, the following officers were elected: Lewis G. Allen, M.D., Kansas City, President; Richard F. Connard, M.D., Emporia, Vice-President; Roger K. Wallace, M.D., Riley County Hospital, Manhattan, Secretary-Treasurer.

ROCHESTER (N. Y.) ROENTGEN RAY SOCIETY

The Rochester Roentgen Ray Society has elected officers for the coming year as follows: President, Theodore Van Zandt, M.D.; Vice-President, Raymond Gramiak, M.D.; Secretary-Treasurer, Robert H. Greenlaw, M.D., 260 Crittenden Blvd., Rochester

20, N. Y. The Society meets the last Monday of each month, September through May.

RADIOLOGIC PHYSICS COURSE COLUMBIA UNIVERSITY, NEW YORK

A one-year course in radiological physics, leading to the degree of Master of Science, is offered under the auspices of the Department of Radiology of the College of Physicians and Surgeons of Columbia University. It is designed to prepare candidates to carry out all the functions of a physicist in a hospital department of radiology; it would also furnish a foundation for those who wish to engage in research or applications in radiologic physics, radiation protection, and dosimetry. The course includes lectures, seminars, conferences, and laboratory work. Topics included are elementary and advanced radiologic physics, electronics, radiation standardization and protection, radioactive isotopes, biostatistics, radiobiology, instrument design, and clinical applications of radiation physics. Prerequisite for admission is a Bachelor's degree with a major or strong minor in physics, or equivalent scholastic background, and a good academic record. A knowledge of general chemistry and general biology is desirable.

As part of its national program for the training of radiological health specialists, the Division of Radiological Health, Public Health Service, has awarded a grant to the University enabling financial assistance to qualified candidates. This aid will be in the form of tuition waiver as well as monthly stipend allowances. Applicants must be citizens of the United States or have filed a Declaration of Intent. Preference will be given to candidates who are sponsored by public health agencies for work in their area of responsibility or in closely related fields.

Inquiries should be addressed to Dr. H. H. Rossi, 630 W. 168th Street, New York 32, N. Y.

UNIVERSITY OF CINCINNATI REFRESHER COURSE IN DIAGNOSTIC ROENTGENOLOGY

The Third Annual Refresher Course in Diagnostic Roentgenology will be conducted June 12-16, 1961, by the Radiology Department of the University of Cincinnati College of Medicine under the direction of Benjamin Felson, M.D. The course will include, in addition to lectures and demonstrations, teaching methods employing audience participation. Further information concerning the course, which is open to radiologists and radiology residents, may be obtained from Jerome F. Wiot, M.D., Department of Radiology, Cincinnati General Hospital, Cincinnati 29, Ohio.

COURSE IN ADVANCES IN CLINICAL RADIOISOTOPE INSTRUMENTATION

A five-day course entitled "Advances in Clinical Radioisotope Instrumentation" will be offered Oct. 23-27, 1961, at the Medical Division of the Oak Ridge Institute of Nuclear Studies, Oak Ridge, Tenn. Designed for physicians and paramedical personnel who already have experience in handling radioisotopes, the course is limited to 40 participants. It will consist of lectures and demonstrations and will cover theory and practical aspects of liquid, crystal, and gas detectors. Topics to be included are circuitry, electronics, data processing, scanning, dosimetry, and calibration.

Application forms and additional information are available from Ralph M. Kniseley, M.D., Medical Division, Oak Ridge Institute of Nuclear Studies, P. O. Box 117, Oak Ridge, Tenn.

FREEDMAN LECTURES UNIVERSITY OF CINCINNATI

On Saturday and Sunday, April 22 and 23, 1961, Dr. Harry Z. Mellins, Professor and Chairman, Department of Radiology, State University of New York Downstate Medical Center, will deliver the thirteenth Annual Joseph and Samuel Freedman Lectures in Diagnostic Radiology at the University of Cincinnati College of Medicine. Radiologists desiring to attend are requested to write Dr. Benjamin Felson, Department of Radiology, Cincinnati General Hospital, for further details.

Letter to the Editor

To Dr. Howard P. Doub
Editor of Radiology

DEAR SIR:

I would like to make a few critical remarks on the article of Mintz and Mattes on bone-free detection of intraocular foreign bodies, appearing recently in *RADIOLOGY* (75: 612-614, October 1960), from an ophthalmological point of view. The authors have clearly shown that a minute foreign body can be detected by the bone-free method of Vogt when ordinary roentgenograms fail to demonstrate any foreign matter. But it is also evident, from the article, that the foreign body was already visible by simple ophthalmologic means, so that the bone-free radiography only corroborated an already firmly established diagnosis.

My objection to the article is that it may lead to the erroneous belief that in cases of *invisible* intraocular foreign bodies (the majority), the same procedure might be followed, with interpretable results. As a matter of fact, such a bone-free exposure will only corroborate the diagnosis of intraocular foreign body, which usually has already been made by use of simple ophthalmologic means (slit-lamp and ophthalmoscope). It is, indeed,

not the *detection* of the foreign body at which the radiologist should aim, but its *localization*. It seems that in the case of Drs. Mintz and Mattes the detection in the roentgenological sense was superfluous, while no attempt was made to localize. As is rightly pointed out, since the Sweet method completely fails for minute foreign bodies, there is a definite need for a *bone-free localization technic*.

We would not venture to criticize the "empty" method of diagnosing a foreign body, as described by Drs. Mintz and Mattes, if we had no better solution to offer. In our Groningen Ophthalmological Clinic, however, we have used with success the following *bone-free localization technic*.

A contact lens (Comberg type), which marks the ocular axis and the corneal rim, is attached to the eye by means of slight suction. This completely prevents any displacement during the roentgenographic study. Exposures are made with the technic of Vogt. From the two resulting photographs a localization can be made with an accuracy within 0.5 mm.

As a complete localization with this new roentgen reference contact lens is in both the "ordinary" and the bone-free exposure a matter of minutes, and as this method, as used in our clinic, is the most simple and exact localization method *known at present*, I thought it worthwhile to draw the attention of your readers to it.

J. WORST, M.D.
University Eye Clinic
(Chief, Dr. H. M. Dekking)
Groningen, Holland

Books Received

Books received are acknowledged under this heading, and such notice may be regarded as recognition of the courtesy of the sender. Reviews will be published in the interest of our readers and as space permits.

NEUROVASCULAR COMPRESSION SYNDROMES OF THE SHOULDER GIRDLE. By LOUIS M. ROSATI, M.D., Professor of Clinical Surgery, New York University Post-Graduate Medical School; Attending Surgeon, Bellevue and University Hospitals, New York, and JERE W. LORD, M.D., Professor of Clinical Surgery, New York University Post-Graduate Medical School; Attending Surgeon, Bellevue and University Hospitals, New York. Modern Surgical Monographs, 3. A monograph of 168 pages, with 27 figures and 14 tables. Published by Grune & Stratton, New York 16, N. Y., 1961. Price \$7.25.

RADIOPAQUE DIAGNOSTIC AGENTS. By PETER K. KNOEFEL, M.D., Professor of Pharmacology, University of Louisville, Louisville, Kentucky. Publication Number 401, American Lecture

Series. A monograph of 158 pages, with 24 figures. Published by Charles C Thomas, Springfield, Ill., 1961. Price \$6.75.

RADIATION PROTECTION AND RECOVERY. Edited by ALEXANDER HOLLAENDER, Oak Ridge National Laboratory, Operated by the Union Carbide Corporation for the United States Atomic Energy Commission. Volume 7, International Series of Monographs on Pure and Applied Biology, Division: Modern Trends in Physiological Sciences. A volume of 392 pages, with figures and tables. Published by Pergamon Press, 122 East 55th St., New York 22, N. Y., 1960. Price \$12.50.

X-RAY MICROSCOPY. By V. E. COSSLETT, M.A., Ph.D., University Lecturer in Physics, Cavendish Laboratory, Cambridge, and W. C. NIXON, M.A., Ph.D., Assistant Director of Research, Engineering Laboratory, Cambridge; formerly A. E. I. Research Fellow, Cavendish Laboratory, Cambridge, England. Cambridge Monographs on Physics. A volume of 406 pages, with figures and tables. Published by the Cambridge University Press, 32 East 57th St., New York 22, N. Y., 1960. Price \$15.00.

RADIOLOGICAL HAZARDS TO PATIENTS. Second Report of the Committee, Ministry of Health, Department of Health for Scotland. A monograph of 114 pages, with 8 figures and 29 tables. Published by Her Majesty's Stationery Office, London, England, 1960. Agents in America: British Information Services, 45 Rockefeller Plaza, New York 20, N. Y. Price \$1.16 postpaid.

VASO-SEMINAL VESICULOGRAHY IN HYPERTROPHY AND CARCINOMA OF THE PROSTATE WITH SPECIAL REFERENCE TO THE EJACULATORY DUCTS: A CLINICAL AND EXPERIMENTAL ROENTGENOLOGICAL STUDY. By GUNNAR WILLER VESTBY. From the Roentgen Department, Ullevål Hospital, Oslo, Norway. A monograph of 194 pages, with 119 figures. Published by Oslo University Press, Oslo, Norway, 1960. Distribution office, United States: 355 North St., Boston 9, Mass. Also published as Supplement 199 to *Acta radiologica*.

SYMPOSIUM ON MAMMALIAN GENETICS AND REPRODUCTION GIVEN AT RESEARCH CONFERENCE FOR BIOLOGY AND MEDICINE OF THE ATOMIC ENERGY COMMISSION, SPONSORED BY THE BIOLOGY DIVISION, OAK RIDGE NATIONAL LABORATORY, OAK RIDGE, TENN., HELD AT GATLINBURG, TENN., APRIL 4-7, 1960. Reprinted from *Journal of Cellular and Comparative Physiology*, Volume 56, Supplement 1, November 1960. A volume of 194 pages, with figures and tables. Published by The Wistar Institute of Anatomy and Biology, Philadelphia, Penna., 1960.

L'ARTHROSE CERVICALE POSTÉRIEURE (ÉTUDE ANATOMO-RADIOLOGIQUE). THE POSTERIOR CERVICAL OSTEO-ARTHRITIS (ANATOMICAL AND RADIOLOGICAL STUDY). DIE HINTEREN HALS-ARTHROSE (ANATOMISCHE- UND RÖNTGENSTUDIE). By S. DE SÈZE, A. DJIAN, C. WELLINGER, and J. LEROY. Travail du Centre de Rhumatologie Viggo-Petersen de l'Hôpital Lariboisière. Foreword by A. Hubault. Iconographie: Supplément international des "Monographies médicales et scientifiques," October 1960, No. 1. An atlas of 80 pages, with 103 figures and text and legends in French, English, and German. Published by Docteur Jean Garnier, 30, rue des Saints-Peres, Paris VII^e, France, 1960.

GASTROENTEROLOGISCHE RÖNTGENPROBLEME: GALLENBLASE, GALLENWEGE, CÔLON. PROBLÈMES GASTRO-ENTÉROLOGIQUES ET RADIOLOGIQUES: VÉSICULE, VOIES BILIAIRES, CÔLON. Edited by E. HAFTER, Zürich, M. RAMSEYER, Lausanne, and J. WELLAUER, Zürich. Bibliotheca radiologica, Supplementa ad "Radiologia clinica," Fasc. 2. A collection of German and French articles, with English summaries, 104 pages, with 64 figures. Published by S. Karger, Basel, Switzerland, 1961. American representative: Albert J. Phiebig, Post Office Box 352, White Plains, N. Y. Price \$5.30.

Book Reviews

MEDICAL PHYSICS. VOLUME III. Edited by OTTO GLASSER, Ph.D., Diplomate in Radiological Physics, American Board of Radiology; Professor of Biophysics, Frank E. Bunts Educational Institute; Head, Department of Biophysics, Cleveland Clinic Foundation; Member, Council on Medical Physics, American Medical Association. A volume of 754 pages, with numerous figures and tables. Published by The Year Book Publishers, Inc., Chicago, Ill., 1960. Price \$25.00.

Volumes I and II of Medical Physics set a high standard that has been maintained in the third. This volume is in no sense a revision of the earlier ones, but rather supplements them. Many new subjects not previously considered have been included, and subjects which have already received attention are brought up to date, with references to the earlier discussions where appropriate. The notable addition in the field of radiology is a 56-page section on radioactive isotopes.

The list of contents contains many familiar names for, as before, the individual contributions are the work of leaders in the respective fields. The discussions, though they have been kept brief, are accurate and complete.

With its two predecessors, this book should be in every medical library, particularly in those of radiologists, whose specialty is more closely allied to physics than that of any other medical group.

THE YEAR BOOK OF RADIOLOGY (1959-1960 Year Book Series; 1960-1961 Year Book Series). RADIOLOGIC DIAGNOSIS. Edited by JOHN FLOYD HOLT, M.D., Professor, Department of Radiology, University of Michigan, and WALTER M. WHITEHOUSE, M.D., Associate Professor, Department of Radiology, University of Michigan. RADIATION THERAPY. Edited by HAROLD W. JACOX, M.D., Professor of Radiology, College of Physicians and Surgeons, Columbia University; Chief, Radiation Therapy Division, Radiologic Service, Presbyterian Hospital, New York, N. Y., and MORTON M. KLIGERMAN, M.D., Professor of Radiology and Chairman of the Department of Radiology, Yale University School of Medicine; Director of Radiology, Grace-New Haven Community Hospital, New Haven, Conn. 1959-1960 Series, 446 pages, with 328 figures; 1960-1961 Series, 442 pages, with 305 figures. Published by The Year Book Publishers, Inc., Chicago 11, Ill. Price, 1959-1960 Series, \$10.50; 1960-1961 Series, \$11.00.

Appearing in yearly succession, the *Year Books of Radiology* pose a recurrent problem for the reviewer who seeks to find new ways of calling attention to the excellence of these volumes. The 1959-1960 and 1960-1961 series continue to afford evidence of the good judgment exercised in the selection from the voluminous literature of contributions to be included. The editors have wisely refrained from attempting to abstract the unabstractable and in a number of instances have contented themselves with merely calling the attention of the interested reader to the original paper.

Dr. Holt and Dr. Whitehouse, in the introduction to the section on Diagnosis in the 1959-1960 series, sum up the situation as it applies to their field:

"A review of the many articles of the past year again indicates the steady progress in our field of specialization: the continued development of technical methods which allow the expansion of peripheral frontiers; the solid filling-in of previously pioneered fields with more comprehensive observations; and the continuous re-evaluation of roentgen signs related to the clinical course and dynamics of disease."

Steady but unspectacular progress has also characterized Radiotherapy, with increasing attention to high-energy equipment in the treatment of malignant disease. Special sections under the heading of Therapy concern Benign Tumors, Isotopes, Radiobiology, Physics, Dosimetry and Treatment Technics, and Radiation Hazards and Injuries.

The first *Yearbook of Radiology* appeared in 1932. The radiologist who has the complete series on his bookshelves has a continuous picture of what has perhaps been the most rapidly developing of the medical specialties.

GLOSSARY OF WORDS AND PHRASES USED IN RADIOLOGY AND NUCLEAR MEDICINE PREPARED FROM VARIOUS SOURCES FOR MEDICAL SECRETARIES, X-RAY TECHNICIANS, MEDICAL STUDENTS AND RESIDENTS IN RADIOLOGY. By LEWIS E. ETTER, B.S., M.D., F.A.C.R., Professor of Radiology and Chief, Radiological Service, Western Psychiatric Institute and Falk Clinic, School of Medicine, University of Pittsburgh; Consultant, Pittsburgh State Tuberculosis Hospital, Leech Farm, Pittsburgh, Penna. With a section on SUGGESTED TERMINOLOGY FOR ROENTGENOLOGICAL REPORTS. Devised by Doctors FISHER, BOVARD, and BACON for the Pennsylvania Radiological Society. Foreword by Olive G. Johnson, A. B., Medical Record Librarian-in-Chief, Health Center, University of Pittsburgh. A volume of 204 pages, with 3 figures. Published by Charles C. Thomas, Springfield, Ill., 1960. Price \$8.50.

Like any rapidly developing science, Radiology has given rise to a vocabulary of its own, in part new and in part adapted from other medical and scientific fields. While over the years many terms have found their way into the general medical dictionaries, for others, having to do with the physical and more technical aspects of the specialty, one must look elsewhere. Dr. Etter has met a real need in assembling in a single volume a simple glossary of words and phrases commonly used in radiology and nuclear medicine.

He has addressed his work to medical secretaries, x-ray technicians, medical students, and residents in radiology. He should include also those responsible for the editing and abstracting of radiological papers and indeed all who follow the literature in an attempt to keep abreast of advances in roentgen diagnosis, radiotherapy, and nuclear medicine.

The definitions are concise and simple but are in general adequate, without lengthy expositions which properly belong in more ambitious works.

Preceding the actual glossary is a section on roentgenologic reports, with suggested terminology, a few pages on the preparation of such reports, and selected samples.

This slight volume is heartily recommended to radiologists and all those associated with the specialty in other capacities.

STUDIES IN RADIOTHERAPEUTICS. By J. S. MITCHELL, C.B.E., M.D., F.R.S., Regius Professor of Physic, University of Cambridge, Cambridge, England. A volume of 274 pages, with figures and tables. Published by Harvard University Press, Cambridge, Mass., 1960. Price \$9.00.

In this book, based upon two courses of lectures—the Edward K. Dunham Lectures at Harvard University and the William Withering Memorial Lectures at The University of Birmingham (England)—the author states that "clinical radiotherapy is still

empirical. It is essential at the present time to provide a basis for the practical application of radiobiology to radiotherapy." His material, therefore, consists less of clinical radiotherapeutic methods and results than of radiobiological experiments contributing to better understanding of underlying principles. He predicts that application of radiobiology to clinical radiotherapy will lead to major improvements.

The first chapter of the work covers experiments designed to elucidate the mechanisms of therapeutic action of ionizing radiations. The second discusses means of increasing the effect of a local dose of radiation, first in tissue cultures and then in animal tumors, with clinical trials of the most promising methods. The last chapter describes the newest high-energy sources of radiation and closes with a discussion of optimum dose and time of treatment.

This is a scholarly, well written book. It will be of interest to radiotherapists and research workers in allied fields.

ISOTOPIC TRACERS: A THEORETICAL AND PRACTICAL MANUAL FOR BIOLOGICAL STUDENTS AND RESEARCH WORKERS. By G. E. FRANCIS, Reader in Biochemistry, St. Bartholomew's Hospital Medical College, W. MULLIGAN, Senior Lecturer in Biochemistry, Glasgow University Veterinary School, and A. WORMALL, Professor of Biochemistry, St. Bartholomew's Hospital Medical College. With a foreword by G. Hevesy. A volume of 524 pages, with numerous figures and tables. Published by University of London, The Athlone Press, London, England, 2nd ed., 1959; Oxford University Press, New York, N. Y., 1960. Price \$8.40.

As the authors say in their Preface, "a modern book dealing with isotopes has a relatively short 'half-life' and must require 'reactivation' from time to time." This second edition of *Isotopic Tracers*, revised and enlarged, includes the advances made in the five years since the original publication. In particular, instrumentation and protection rules have been brought up to date.

The book is divided into two parts. The first, and by far the larger, is titled "Theoretical Considerations," but it is very practical theory. The user of tracer isotopes will readily perceive its applications to his problems. Biological aspects are stressed, making the book useful to physicians.

In "Part II, Practical Course," experiments on mice and rabbits are outlined which are good preparation for work on man. Some of these "exercises" might be performed with profit by the radiology resident.

Appendixes include tables of isotopes with physical and biological data, a glossary of words and phrases, typical rules for a biochemical tracer laboratory, directions for various laboratory procedures, and decay factors for the more commonly used isotopes. Any isotope laboratory engaged in biological

applications of tracers will find this book a valuable addition to its library.

PRINCIPLES OF RADIOISOTOPE METHODOLOGY. By GRAFTON D. CHASE, Ph.D., Associate Professor of Chemistry, Philadelphia College of Pharmacy and Science, with the cooperation of JOSEPH L. RABINOWITZ, Ph.D., Assistant Professor of Biochemistry, University of Pennsylvania. A volume of 286 pages, with numerous figures and tables. Published by Burgess Publishing Co., Minneapolis, Minn., 1959. Price \$6.00.

This book is a laboratory manual from which an instructor can select experiments of varying difficulty, according to the background of his class. It is written primarily for research workers making use of radioisotopes in such fields as chemistry, biology, physiology, etc. There is very little discussion of theory; this would have to be supplied by lectures or supplementary reading.

The experiments are not particularly applicable to the problems confronting the radiology resident in his study of medical applications of radioisotopes.

MEDICAL X-RAY TECHNIQUE: PRINCIPLES AND APPLICATIONS. By G. J. VAN DER PLAATS, former Professor of Radiology, University of Groningen, Groningen, Netherlands. A volume of 480 pages, with 213 figures. Published by the Macmillan Co., New York, 1959. Price \$10.00.

G. J. van der Plaats, Professor of Radiology at Groningen University in Holland, is well prepared to write a textbook on x-ray technic for teaching purposes. He has had a lifelong interest in this subject and, because of this, covers his subject thoroughly. His method of presentation is also good, with a liberal use of diagrams and some roentgenographic reproductions.

The text includes chapters containing basic and detailed information on the origin of x-rays, image formation, laws of projection, and radiographic technic in both routine and special procedures. The various types of apparatus are described, together with the biological effects of radiation and the methods of irradiation producing these effects. Dosages for superficial, deep, and contact therapy receive attention, and a chapter on treatment with the radioactive elements makes the text currently informative. A final chapter considers radiation hazards and protection.

This volume is an excellent handbook for x-ray technologists and medical students particularly interested in radiology.

ANATOMY AND PHYSIOLOGY FOR RADIOGRAPHERS. By J. E. BLEWETT, M.D., D.M.R., F.F.R., Director of Diagnostic Radiology Department, King's College Hospital, London, and the Belgrave Hospital for Children, and A. M. RACKOW, B.Sc.,

M.B., D.M.R.E., Assistant Director of Diagnostic Radiology Department, King's College Hospital, London, and the Belgrave Hospital for Children. A volume of 364 pages, with 133 figures and 22 plates. Published by Butterworth & Co. Ltd., London, England, and Washington, D.C., 1960. Price \$7.50.

This book is designed to take fundamental biology and physiology and incorporate them into an integrated body of knowledge for persons without a medical background. The second chapter deals with cell structure and functions. The next two chapters treat of the pathological-physiological aspects of infections and neoplasms. A systematic functional approach to the locomotor system follows, with excellent line drawings. Topographical anatomy, with definition of useful landmarks, is taken up in a short chapter that is well worth perusal by every technician. The circulatory and respiratory systems are well covered, with the principles underlying their study. The alimentary tract, genitourinary tract, ductless glands, and lymphatic and nervous systems are treated in separate chapters.

It is unfortunate that the good glossy prints, presumably for technical reasons, are separated from the text to which they apply. However, the line drawings integrated with the text are excellent. This is a good book with an academic approach.

DIE OKZIPITALE DYSPLASIE. By DOZ. DR. HERMANN SCHMIDT and DR. ERICH FISCHER, Med.-Strahleninstitut der Universität Tübingen. Heft 9, Zwanglose Abhandlungen aus dem Gebiet der normalen und pathologischen Anatomie, edited by Prof. Dr. W. Bargmann, Direktor des Anatomischen Instituts der Universität Kiel and Prof. Dr. W. Doerr, Direktor des Pathologischen Instituts der Universität Kiel. A monograph of 70 pages with 108 illustrations on 69 figures. Published by Georg Thieme, Herdweg 63, (14a) Stuttgart, Germany, 1960. Price DM 35.— (\$8.35); to subscribers to the series DM 28.— (\$6.70). Distributed in the United States and Canada by the Intercontinental Medical Book Corporation, New York 16, N. Y.

One problem of importance in the study of the occipital region of the skull is the diagnosis of basilar impression. The present thesis is concerned with basilar impression particularly in its developmental form, excluding the secondary varieties caused by fracture, osteoporosis, and Paget's disease. The authors seek to answer four questions:

- What are the developmental anomalies that affect the occipital bone?
- What are their roentgen appearances?
- How do they lead to basilar impressions?
- How do they affect the position of the cervical vertebrae?

Formerly the diagnosis of basilar impression sufficed in itself as an expression of occipital deformity. Actually, in terms of occipital bone dysplasia, basilar impression is only one sign, perhaps of many different disturbances. The fundamental abnormality is a developmental bone dysplasia; the cause of this may be obscure, but it nevertheless represents the underlying process behind the roentgen signs. The developmental deficiency may affect the pars basilaris, the occipital condyles, or the lateral masses. It may or may not be associated with atlas assimilation. Platybasia is frequently associated but does not in itself constitute basilar impression.

A large number of "help lines" have been developed for evaluation of these abnormalities, and most of these are useful, though merely as "help lines," and not as diagnostic entities in themselves.

This is an excellent treatise, brief, practical, and well illustrated. The four questions set by the authors are quite adequately answered, which is the reason the monograph can be recommended for careful study.

LES ISOTOPES RADIOACTIFS. Rapports présentés au XXXII^e Congrès français de médecine, Lausanne, 1959 (Association des médecins de langue française). Président du Congrès: Professeur A. Vannotti. A volume of 116 pages, with figures and tables. Published by Masson et Cie, 120 Blvd. Saint-Germain, Paris VI^e, France, 1959.

The reports of radioactive isotopes presented at the Thirty-second French Congress of Medicine held in Lausanne, Switzerland, in 1959, are assembled in a paper-bound volume of something over a hundred pages. The subjects include: Artificial Isotopes in Medicine and Biologic Applications of Radioactive Iodine, by Jean Roche and Raymond Michel, Collège de France, Paris; Metabolism of Electrolytes in Man Studied with the Aid of Radioisotopes, by G. Milhaud, E. Loizeau, and C. Nagant de Deuxchaisnes, Institut Pasteur, Paris, et Clinique thérapeutique universitaire, Geneva, Switzerland; Histoautoradiography and Cellular Metabolism of Nuclear Acids, by M. Chèvremont, Liège, J. Brachet, Brussels, and H. Firket, Elisabethville; The Exploration of the Biliary Tract by Labelled Iodine Derivatives, by André Chevallier, Strasbourg; The Use of Radioisotopes in Hematologic Research, by G. Hemmeler, Lausanne; Protection Against Irradiation and Treatment of Its Effects, by Jean-Marie Loisele, Quebec, Canada; Application of the Kinetics of Removal of a Radioactively Tagged Protein Complex from the Blood in the Study of Phagocytic Action of the Reticuloendothelial System and of Hepatic Blood Flow in Normal and Cirrhotic Patients, by B. N. Halpern, G. Bozzi, B. Delaloye, G. Péquignot, C. Stiffel, and D. Mouton, of Paris.

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ROENTGEN DIAGNOSIS

The Role of Diagnostic Roentgenology in Medicine.

Max Ritvo. *New England J. Med.* 262: 1201-1209, June 16, 1960. (Boston City Hospital, Boston, Mass.)

The Annual Discourse to the Massachusetts Medical Society for the year 1960, delivered by the Director of Radiology and Roentgenologist-in-Chief of the Boston City Hospital, affords a kaleidoscopic review of the history, present implications, and future applications of diagnostic roentgenology in the practice of medicine.

The discovery of the x-ray is universally regarded as one of the most significant events in medical annals. Every field of medicine has felt the impact and enjoyed the benefits of x-ray diagnosis.

The author elaborates by discussing the scope of diagnostic roentgenology, the dependability of x-ray examinations, and the limitations of the method. Turning to the hazards of radiation, he presents brief comments concerning leukemogenesis, carcinogenesis, the effect on the life span, and genetic effects. Caution is urged lest blind fear of x-ray exposure negate the positive benefits of diagnostic studies.

The role of the roentgenologist as a medical specialist is considered. His indispensable position in teaching is pointed out with special attention to the several different avenues of approach depending upon the recipients, whether they be those specializing in the field, undergraduates, graduates, or those in other fields of medicine.

The possibility of future changes in equipment lead to speculation as to the applications of television, image intensification, cineradiography, body-section radiography, and xeroradiography. There is brief consideration of the expanding field of angiography, use of x-rays in research, and the applications of technics of automation to the daily practice of diagnostic roentgenology.

Five roentgenograms. JOHN F. RIESER, M.D.
Springfield, Ohio

THE HEAD AND NECK

Familial Idiopathic Cerebral Calcifications in Childhood. Johannes C. Melchior, Clemens E. Benda, and Paul I. Yakovlev. *J. Dis. Child.* 99: 787-803, June 1960. (Walter E. Fernald State School, Box C, Waverley 78, Mass.)

Calcifications in the brain occasionally found in infants or appearing gradually during childhood are associated with various conditions, some of which have firmly established clinical-anatomical patterns, e.g., tuberous sclerosis, angiomas, toxoplasmosis, hypoparathyroidism, cytomegalic inclusion-body disease, cysticercosis, and certain tumors. The term "idiopathic non-arteriosclerotic calcifications of the brain" has been applied to a very particular form of cerebral calcification; this condition is often referred to as "Fahr's disease," although it was known long before the time of Fahr.

The authors have studied two families in which 3 and 2 children, respectively, were affected with idiopathic non-arteriosclerotic calcifications of the brain. In each family one patient died, and a thorough autopsy examination was performed. All 5 patients were undersized and underweight. The clinical manifestations showed a surprising uniformity, consisting of mental retardation with progressive deterioration, epilepsy, dysarthria, extrapyramidal motions, Magnus-de Kleijn tonic

neck reflexes, dolichocephaly associated with microcephaly, hypoplasia of the lower extremities with spastic rigidity, and limited use of the upper extremities.

Roentgen examination of the skull showed patchy calcifications, which were particularly dense in the basal ganglia but were also visualized in the cerebral cortex and in the cerebellum. Occasionally the calcifications took the form of fine dust-like particles scattered diffusely in an intracerebral position.

A review of the literature dealing with intracranial calcifications in infants and young children presents many observations which are helpful in the differential diagnosis. The appearance of the cotton-ball calcifications in tuberous sclerosis is rather typical. The convoluted double-lined shadows seen in hemangiomas (the Sturge-Weber syndrome) or the small, dust-like patches of calcifications in the brain in toxoplasmosis, however, may resemble closely the findings in idiopathic non-arteriosclerotic calcifications of the brain. Of the rarer conditions associated with patchy calcifications, cytomegalic inclusion-body disease and hypoparathyroidism must be kept in mind. The calcifications in a brain tumor are likely to be more massive, focalized, and not diffuse, and are usually associated with a different type of clinical history and course than observed in the authors' patients.

The histologic findings in the cases which came to autopsy are described.

The authors conclude that the association of idiopathic non-arteriosclerotic calcifications of the brain with severe growth disturbance and microcephaly, and the familial incidence, suggest a specific metabolic disorder of a yet unknown nature.

Three roentgenograms; 13 photomicrographs; 2 tables.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Adenoma of the Parathyroid Gland in Children.

Report of Case and Brief Review of the Literature. Robert B. Nolan, Alvin B. Hayles, and Lewis B. Woolner. *J. Dis. Child.* 99: 622-627, May 1960. (The Mayo Clinic, Rochester, Minn.)

An eleven-year-old white girl was admitted to the Mayo Clinic for study because of a peculiar intermittent alopecia, which began six years earlier, involving particularly the scalp and eyebrows. Progressive denting, thickening, and flaking of the fingernails and toenails had been noticed for one year. Physical examination disclosed no abnormalities except those of the hair and nails and slight obesity. Significant laboratory findings were persistent moderate elevation of serum calcium (13 and 13.1 mg. per 100 ml. on successive examinations); mild depression of serum phosphorus (2.8 and 2.9 mg.); alkaline phosphatase, 49 and 57.2 King-Armstrong units. Excretion of calcium in the urine was 290 and 298 mg. on successive days when the child was on a diet containing 200 mg. of calcium daily. Roentgen examination of the chest and a skeletal survey revealed no abnormalities.

At surgical exploration, a single adenoma weighing 120 mg. was removed from the right superior parathyroid region. The postoperative course was uncomplicated, and at the time of the report the child was in good health. Serum calcium and phosphorus levels had reverted to normal, but there had been no regrowth of hair in the eyebrows, and the fingernails, though

more rounded, were still abnormal. Histologic study of the parathyroid tumor showed a uniform pattern of chief cells throughout, with a definite glandular pattern in some areas.

The authors reviewed the literature and were able to find reports on only 22 children with proved hyperparathyroidism associated with parathyroid adenoma. The pertinent laboratory and clinical findings in these cases are tabulated. Eighteen of the 22 children had roentgen evidence of skeletal involvement (subperiosteal reabsorption of bone, seen most frequently along the margins of the middle phalanges, and disappearance of the lamina dura). Radiopaque renal calculi were observed in 6 children. It is interesting that none of these important radiographic findings was demonstrated in the authors' case. No child has been reported as having a malignant tumor arising in the parathyroids.

One photograph; 1 photomicrograph; 2 tables.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Vertebral Arteriography of Benign Tumors. A. Isfort. *Fortschr. a. d. Geb. d. Röntgenstrahlen* 92: 676-689, June 1960. (In German) (Chirurgische Klinik und Poliklinik der Universität Münster i. Westf., Germany)

The author's technic of vertebral arteriography is described briefly. The importance of this procedure in the diagnosis of tumors and vascular abnormalities of the posterior cranial fossa is emphasized. The indications are as follows: (1) evidence of obstructive hydrocephalus on carotid arteriograms; (2) negative carotid arteriograms in the presence of increased intracranial pressure or subarachnoid hemorrhage; (3) a clinical picture which could be due to a vascular disturbance of the cerebellum. A stellate ganglion block is performed on all patients not under deep narcosis, to prevent vasospasm and a possible erroneous diagnosis of cerebellar apoplexy.

The angiographic appearances of benign tumors of the posterior cranial fossa are described by means of actual examples. In all cases displacement of normal vessels was shown. Some tumors were delimited by a vascular margin. Tumor vessels lead to an extensive, homogeneous contrast opacification of the neoplasm. For comparison, the characteristics of malignant tumors are described and illustrated by a medulloblastoma. Here pathologic vessels of variable caliber, arteriovenous anastomoses, lacunae, corkscrew vessels, and shunting through the tumor are frequent findings.

The author emphasizes the value of routine views in three planes (anteroposterior, lateral, and basal) to demonstrate not only the tumor but also the arterial supply. The latter is of considerable importance to the surgeon.

[The arteriograms reproduced in this paper are of exceptionally good quality and clearly demonstrate the findings.—E. A. C.]

Nineteen roentgenograms; 3 photographs.

EUGENE A. CORNELIUS, M.D.
Houston, Texas

Carotid-Basilar Anastomosis Associated with Multiple Aneurysms and Other Anomalies. H.-St. Meyer and G. Busch. *Fortschr. a. d. Geb. d. Röntgenstrahlen* 92: 690-693, June 1960. (In German) (Universitäts-Nervenklinik der Charité Berlin, Germany)

This is a report of a case of carotid-basilar anastomo-

sis associated with multiple aneurysms and other anomalies.

A 24-year-old nurse with congenital cleft palate was referred for neurologic investigation following two subarachnoid hemorrhages three months apart. Hypertension was present. Routine skull examination and a pneumogram showed no abnormalities. The excretory urogram was negative.

A right carotid arteriogram demonstrated a vessel of the caliber of the internal carotid extending from the "ganglionic segment" (C₅ according to Fischer) of the right internal carotid artery to the basilar artery between the anterior inferior and posterior inferior cerebellar branches. The point of origin of the anastomotic vessel from the carotid suggested a primitive trigeminal artery whereas its low point of junction with the basilar corresponded to that of the primitive acoustic artery. Aneurysms were demonstrated, arising from three arteries: the right anterior cerebral, the basilar, and an occipital branch of one posterior cerebral. There was a uniform narrowing of the proximal (A₁) portion of the left anterior cerebral artery. Sclerotic changes were present in the left posterior temporal artery. A right-sided jacksonian seizure occurred during injection of the medium, followed by transitory paresis of the right hand and aphasia.

During the following weeks there were two episodes of loss of consciousness with transitory residual paresis of the right hand and exaggerated deep reflexes on that side. Electroencephalographic changes confirmed the clinical impression of vascular insufficiency of the left cerebral hemisphere.

Treatment was aimed at avoiding the dangerous extremes of low and high blood pressure.

Three roentgenograms; 1 diagram.

EUGENE A. CORNELIUS, M.D.
Houston, Texas

Asymmetric Roentgenography of the Vocal Chords. Ákos Kovács. *Acta radiol.* 53: 426-432, June 1960. (Simmelweis Hospital, Budapest, Hungary)

The author describes a method for demonstrating the right and left vocal cords separately, in comparable views. If a vocal cord is to be visualized in its full depth, an asymmetric oblique projection must be used. The cord to be examined should be positioned so that the central ray strikes it as it lies outlined by air. Care must be taken that the soft parts are not masked by bone.

The patient is seated, with the head rotated away from the side to be examined; the slight torsion produced upon the larynx brings the vocal cord of this side into approximately the frontal plane and out of the way of the spine. The patient holds a special combined film holder and device for displacing the larynx. He takes a deep breath, lets it out, and holds it in expiration, this having the effect of moving the larynx upward. He then presses the device into the soft parts of the neck and the exposure is made. The central ray is directed from behind at an angle of between 30° and 40° with the sagittal plane. The procedure is repeated for the opposite side. Phonation studies, as well as Valsalva and Mueller maneuvers, are readily performed.

One advantage of the procedure is that it permits the demonstration of the vocal cords at rest, making it a satisfactory complement to the unphysiologic laryngoscopic examination. The method is particularly valuable for showing proliferation below the vocal cords

since their inferior aspects are usually beyond the range of the laryngoscope.

Thirteen roentgenograms; 10 drawings.

CAPT. JOHN R. BROADWATER, M.C.
Lackland AFB, Texas

THE CHEST

A 5-Year Follow-Up of Roentgenographically Detected Lung Cancer Suspects. Lewis W. Guiss. *Cancer* 13: 82-90, January-February 1960. (University of Southern California School of Medicine, Los Angeles, Calif.)

In 1950 chest minifilms of 1,867,201 persons in Los Angeles County (California) were obtained. From these minifilms, 3,500 "lung tumor suspects" were found, were incorporated into a tumor registry, and have been followed. The present and final report is a continuation of an earlier 3-year summary (*Cancer* 8: 219, 1955. *Abst. in Radiology* 66: 129, 1956).

Of the 1,955 persons in whom cancer was ruled out in the three-year study, 35 were found to have pulmonary neoplasms, 19 of which were bronchogenic cancers.

Of 96 patients thought to have metastatic carcinoma, 84 are dead, 6 are lost to follow-up, 6 were living and well seven years after the minifilming. It is thought that these last 6 had other diseases, probably inflammatory, which mimicked carcinoma on the films.

Of 293 with clinically benign neoplasms, untreated at the time of the earlier report, 61 were now lost, 8 had had successful surgery for granuloma, 33 were dead—7 of bronchogenic carcinoma, 5 of carcinoma of other organs, 21 of intercurrent disease. Two patients with extrapulmonary thoracic malignant disease died. In 8, all living at the time of the report, benign tumors were resected.

The final figure for confirmed bronchogenic carcinoma in this group was 244.

When the absolute cure rate for all bronchogenic cases in the registry is calculated, merging both determinate and indeterminate figures, including all treated and untreated cases (total 244), the absolute cure rate becomes 9.9 per cent. This compares favorably with other reported series and suggests that earlier treatment is the factor in cure. The size of the pulmonary lesion, providing it is surgically resectable, has no definite correlation with either symptomatology or prognosis, but the asymptomatic patient has three times the chance of cure as does the patient with presurgery symptoms.

Periodic repetitive roentgenography of the chest, though expensive, is currently the only generally available and practical method of detecting lung cancer before it becomes symptomatic and incurable. If screening programs were restricted to selected groups and to men over forty-five years old, the percentage yield in lung cancer might be increased immensely.

Nine tables.

A Retrospective View of Survey Photofluorograms of Persons with Lung Cancer. Lewis W. Guiss and Patricia Kuenstler. *Cancer* 13: 91-95, January-February 1960. (University of Southern California School of Medicine, Los Angeles, Calif.)

A retrospective study was undertaken on those patients whose minifilms had been obtained in the 1950 Los Angeles County chest roentgenographic survey (see preceding abstract). The films, with other miscellane-

ous roentgenograms mixed in, were reread in random order by a diagnostic radiologist, a diplomate of the American Board of Radiology, who had had extensive experience with minifilms. At no time did the reviewer have access to the original reading of the minifilms.

Although the survey included 60 per cent of all people over fifteen in Los Angeles County, only 21.5 per cent of those subsequently dying of lung cancer had such minifilms. Initial abnormal reports had been made for 162 of 258 patients dying in the first two years of the study; of only 49 of 390 dying in the last two years. On review of the "negative" films, major errors of underreading were revealed. Although half the minifilms originally read as negative were reported the same on both reviews, one quarter were judged abnormal once and the final quarter were considered definitely abnormal on both occasions. From these findings it must be assumed that significant changes were either overlooked or deliberately underread.

It is concluded that there may be great variation in the interpretation of pulmonary minifilms, depending on the bias of the individual reader and intentional policies of "underreading" or "overreading." Differences inherent in reporting may be significantly exaggerated by reader fatigue, error, and omission of second reviews. Dual reading of the "negative" films in this study would have resulted in definite "abnormal" reports in one-fourth of them and "questionable abnormal" reports in a like number; dual reading of the "positive" films would only have confirmed the presence of disease.

There is great need for establishing definite standards by which survey minifilms may be more accurately interpreted. Scientific criteria must be developed and applied to the procedure.

One graph; 6 tables.

Physiologic and Clinical Aspects of Pulmonary Alveolar Proteinosis. William Fraimow, Richard T. Cathcart, and Richard C. Taylor. *Ann. Int. Med.* 52: 1177-1194, June 1960. (R. T. C., Jefferson Medical College Hospital, Philadelphia 47, Penna.)

The authors review the literature on pulmonary alveolar proteinosis, with particular emphasis on the mode of production of the severe pulmonary insufficiency frequently found in this disease, and report 2 cases. In both of their patients an alveolar-capillary block was demonstrated.

The features of the alveolar-capillary block syndrome consist of a restrictive pattern of ventilation with relative preservation of ventilatory ability, hyperventilation, arterial oxygen unsaturation, which may be minimal at rest but may increase markedly on exercise, and a normal ability to excrete carbon dioxide. It has been noted that this syndrome morphologically has been accompanied by some process involving the interalveolar interstitium, either inflammatory, granulomatous, or neoplastic in nature. Diffusion problems have also been observed where there was a marked reduction in the capillary bed. In alveolar proteinosis, however, neither of these situations exists. A relative lack of cellular infiltration in the interalveolar septa is characteristic, and the capillary bed is unaltered. The diffusion problem thus appears to be due to the presence of the proteinaceous material within the alveolar spaces, together with changes in the size and number of alveolar septal cells.

That the problem in diffusion is not the sole cause of cyanosis in this disease was demonstrated in 2 patients by the fact that administration of an increased concentration of oxygen did not result in full arterial saturation. This must be the result of shunting of blood from the venous to the arterial side. A histologic explanation for the presence of this physiologic shunting is that the proteinaceous material is extensive enough to plug completely the smaller bronchioles as well as the alveoli; there is blood flow but no exchange of gases in these areas.

At present the diagnosis of pulmonary alveolar proteinosis must of necessity be made by examination of lung tissue, although a presumptive diagnosis can be entertained clinically. The clinical course in most cases has been characterized by an insidious onset, with slow progression of dyspnea, weakness, fatigue, increased cough, and weight loss. X-ray findings are helpful, most typically consisting of a fine, soft, diffuse, bilateral, perihilar-radiating, floccular-appearing density.

Steroid therapy does not appear particularly effective in this disease, and indeed several fatalities have been attributed to secondary fungal infections, aided and abetted by the use of steroids and antibiotics. Since steroids are often successfully employed in the treatment of other diseases associated with alveolar-capillary block syndrome, such as berylliosis, Hamman-Rich syndrome, sarcoidosis, and scleroderma, it becomes imperative that every effort be made to arrive at a definite diagnosis in cases of diffuse and puzzling pulmonary changes before resorting to the empiric use of corticoids and broad-spectrum antibiotics.

Six roentgenograms; 4 photomicrographs; 3 tables.

CHARLES M. GREENWALD, M.D.
St. Cloud, Minn.

Pulmonary Alveolar Proteinosis. William R. Edmondson and J. Brewster Gere. *Ann. Int. Med.* 52: 1310-1318, June 1960. (W. R. E., 503 Central Ave., East Orange, N. J.)

The authors report the clinical, laboratory, radiographic, and histologic findings in a 53-year-old Negro male with pulmonary alveolar proteinosis. This is the third recorded occurrence of the disease in an American Negro.

Pulmonary symptoms had been present some eighteen months prior to diagnostic thoracotomy. X-ray examination showed a soft confluent infiltrate in both lung bases, with the upper lungs essentially clear. A bronchogram disclosed no alterations of the visualized portions of the bronchial tree.

The etiology of this disease remains unknown, and the diagnosis can be established only by lung biopsy. As of now there is no specific therapy and treatment is limited to symptomatic measures.

Three roentgenograms; 1 photomicrograph; 1 table.

CHARLES M. GREENWALD, M.D.
St. Cloud, Minn.

Pleural Calcification as a Roentgenologic Sign of Non-Occupational Endemic Anthophyllite-Asbestosis. Raimo Kiviluoto. *Mineralogical Appendix.* Olavi Kouvo. *Acta radiol. Suppl.* 194, 1960. (Central Hospital of Northern Karelia, Finland)

During a thirty-three-month-period, at the Central Hospital of Northern Karelia (Finland), 126 cases of pleural calcification were found in 39,000 roentgeno-

grams of the chest. Hemothorax, tuberculosis, and empyema could be excluded as the cause. Calcification resulting from those conditions usually occurs unilaterally and is situated on the visceral pleura; in most cases, the calcium deposit has a consistent shell-like appearance and is found in the lateral part of the lung. Interlobar calcification is sometimes present. Marked pleural thickening and displacement of the intrathoracic organs are frequent, as well as deformity of the chest.

The calcification in the cases seen by the author was of a distinctly different character. The calcium deposit was located on the parietal pleura and in most instances was bilateral, appearing roentgenographically as solitary or confluent spots or figures. Besides the calcium plaques on the inner chest wall, basal and mediastinal calcification was often observed, but in no instance was there interlobar calcification. In early cases the deposits were located in the anterolateral part of the chest, where excursion during respiration is greatest. Clinically, the patients had neither subjective nor objective respiratory symptoms.

From the roentgenologic point of view, the most probable explanation for the calcifications appeared to be a pneumoconiosis. No history of occupational exposure to dust was obtained, but it was discovered that all but 8 of the 126 patients lived or had formerly lived in Kuusjärvi or a neighboring commune. Two open anthophyllite-asbestos mines are located at about the center of this area. Asbestos inhalation was therefore considered to be the etiologic factor for the calcifications, and in a case which came to autopsy fibrous material found in the lungs proved to be anthophyllite asbestos. It is thought that, because of their shape, the inhaled asbestos fibers may remain attached to the lung surface and visceral pleura. During respiration they are immobile in relation to the lung and visceral pleura but move in relation to the parietal pleura, which may be scratched by their protruding ends. Small hemorrhages and mechanical irritation result. The hemorrhages coagulate and organize, and the collagenous tissue becomes necrotic and slowly calcifies.

The damage caused by anthophyllite asbestos in the author's cases is different both clinically and roentgenologically from the well known occupational asbestosis. In the present series there was a low incidence of usually mild pulmonary fibrosis. Not a single case of pulmonary cancer was encountered.

Twenty-five roentgenograms; 12 tables.

ARCH W. TEMPLETON, M.D.
The Henry Ford Hospital

Middle-Lobe Atelectasis Due to Endobronchial Sarcoidosis, with Hypercalcemia and Renal Impairment. Gerald J. Goldenberg and Richard H. Green-span. *New England J. Med.* 262: 1112-1116, June 2, 1960. (University of Minnesota Medical School, Minneapolis 14, Minn.)

Originally the term "middle-lobe syndrome" was applied only to bronchial narrowing due to external compression by enlarged hilar lymph nodes. More recently it has been applied as well to bronchial narrowing due to intrinsic disease in the bronchial wall proper. The authors prefer the term "middle-lobe atelectasis," to include all cases, whether produced by extrinsic or intrinsic compression. A case of endobronchial sarcoidosis causing middle-lobe atelectasis is reported, and 6 cases from the literature are discussed

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The authors' patient was a 66-year-old woman with a two-year history of dyspnea, pain in the left anterior aspect of the chest for three months, and wheezing respirations for two months. X-ray examination revealed a collapse of the right middle lobe. Laminography confirmed this finding and showed an obstruction of the middle-lobe bronchus. At bronchoscopy, erythema was observed about the middle-lobe orifice. Bronchography demonstrated an obstruction of the middle-lobe bronchus, 1.5 cm. from its origin. Biopsy of the bronchial mucosa revealed irregular noncaseating granulomas in the submucosa; special stains for acid-fast organisms and fungi were negative. A Mantoux test (1:100) was negative, as were skin tests for histoplasmosis, coccidioidomycosis, and blastomycosis. There was hypercalcemia; renal-function tests indicated marked impairment. Liver biopsy revealed normal hepatic tissue; a renal biopsy showed tubular atrophy, nonspecific fibrosis, and hyalinization of glomeruli but no calcareous deposits.

While benefits of steroid therapy in pulmonary sarcoidosis are likely to be only temporary, in the case under discussion, treatment with steroids was accompanied by disappearance of symptoms, partial alleviation of bronchial obstruction, diminution of lymphadenopathy, reduction of the serum calcium to normal, and improvement of renal function.

Four roentgenograms; 2 photomicrographs; 1 photograph.

JOHN F. RIESSER, M.D.
Springfield, Ohio

The Calcified Hilar Node: Its Significance and Management. A Review. John Storer and Ralph C. Smith. *Am. Rev. Resp. Dis.* **81**: 858-867, June 1960. (Huron Road Hospital, Cleveland, Ohio)

Calcification of mediastinal lymph nodes is common. Until recent years tuberculosis was thought to be the most frequent cause, but in the Ohio Valley, where histoplasmosis is endemic, it has been found that hilar node calcification is even more often related to histoplasmosis. Although a calcified node may be in juxtaposition to any intrathoracic structure, the organs most frequently involved in complications are the esophagus, superior vena cava, and the tracheobronchial tree.

The calcified node in contact with the bronchus may gradually erode its wall, and fragments may be coughed up as bronchial stones. Recurrent hemoptysis may also occur during the course of the erosion, and a chronic cough may be produced by the associated inflammatory process in the bronchus. Compression of the bronchi by a node may also lead to partial obstruction, with inflammatory changes in the nondraining area. Eventually atelectasis, bronchiectasis, and fibrosis may develop. Such involvement of the middle lobe with its attendant complications has been called the middle lobe syndrome.

Traction diverticula of the esophagus usually occur at the level of the carina and point anteriorly. They originate from traction produced by local inflammatory disease, usually in a lymph node. During the initial period of lymphadenitis, the surrounding tissues become fixed; as the node becomes calcified, it may be stuck fast to a diverticulum on one side and to a bronchus on the other. Occasionally erosion of both the esophagus and the bronchus may result in a bronchoesophageal fistula. A case is presented to illustrate this complication. Surgical removal of the middle lobe, which was involved by a chronic inflammatory

process, and amputation of the esophageal diverticulum and closure of the esophagus corrected the condition.

Obstruction of the superior vena cava may also be produced by an adjacent calcified node (or nodes). Partial obstruction usually antedates a complete block and can be demonstrated by venography. An illustrative case is presented. The patient had paroxysms of coughing precipitated by motion, and he experienced coughing every morning while shaving his neck. Physical examination showed some prominence of the veins of the upper extremities. The cough could be precipitated by extension of the head. A roentgenogram of the chest disclosed a calcified mass adjacent to the trachea; a tracheogram revealed erosion of the tracheal cartilage by this mass. The entire symptom complex was thought to be due to tracheal compression and erosion and slight caval compression. Surgical removal of the mass relieved the symptoms.

As a result of their experience, the authors believe that the patient with hilar node calcification should be studied with respect to possible related clinical manifestations. Esophagrams, bronchograms, and laminagrams may demonstrate the anatomic relationship of the calcified mass to the bronchus, esophagus, or trachea; venography will reveal the relationship to the vena cava. In many cases, early aggressive treatment prevents the development of serious complications.

Twelve roentgenograms; 1 photograph

JOHN H. JUHL, M.D.
University of Wisconsin

The Effect of Intravenous Paraldehyde as Recorded by the Chest X-Ray Film. A Case Report. Jerome A. Gold, Robert C. Garcia, and John W. Davis. *Dis. of Chest* **37**: 453-455, April 1960. (J. A. G., U. S. Naval Hospital, Brooklyn, N. Y.)

The administration of paraldehyde by the intravenous route is rarely, if ever, indicated. A death has been recorded five hours following the intravenous injection of 33 c.c. and fatalities are known to have occurred after oral administration of 35, 75, and 120 c.c. and after rectal administration of 12 and 31 c.c.

A case is presented which demonstrates the unusual pulmonary manifestations which were observed in a 21-year-old healthy man after the intravenous use of only 5 c.c. of paraldehyde for hyperexcitability. The immediate clinical reaction consisted in a short period of apnea, severe cough, tachycardia, and hypotension. A chest roentgenogram, taken thirty minutes after the injection, revealed a bilateral increase in the bronchovascular pattern. Scattered throughout both lung fields were multiple small nodular densities compatible with pulmonary edema and congestion. A chest film taken thirty-six hours later showed complete clearing of the pulmonary lesions. The patient was asymptomatic, and the lung fields were normal to percussion and auscultation. Treatment was solely supportive.

Five roentgenograms. GORDON L. BARTEK, M.D.
Grand Rapids, Mich.

Misleading Thoracic Roentgenograms. Cardiovascular Abnormalities That May Simulate Diseases of the Lungs, Bony Thorax, or Mediastinum. Corrin H. Hodgson, John A. Callahan, Andre J. Bruwer, and Arthur H. Bulbulian. *Arch. Int. Med.* **105**: 277-297, February 1960. (Mayo Clinic, Rochester, Minn.)

This article is actually a collection of chest roentgeno-

grams obtained in some cardiovascular conditions in which the pictures simulate those of diseases of the lungs, bony thorax, or mediastinum. Examples are grouped in the following categories: Shadows produced by abnormal aortic contours, shadows suggesting intrathoracic tumor, shadows produced by intrathoracic fluids, and tumors of diverse origin and complexity.

The films were first shown as a scientific exhibit in the Section on Diseases of the Chest at the meeting of the American Medical Association, San Francisco, 1958.

Forty roentgenograms; 20 photographs.

THE HEART AND BLOOD VESSELS

Approach to the Roentgenologic Diagnosis of Congenital Heart Disease. Owings W. Kincaid. J. A. M. A. 173: 637-647, June 11, 1960. (The Mayo Clinic, Rochester, Minn.)

In 75 per cent of patients with congenital heart disease, the type of malformation present can be accurately determined and its operability assessed by correlation of the history, physical examination, electrocardiographic findings, and conventional roentgenographic and fluoroscopic findings. In the remaining 25 per cent, additional information must be obtained by special procedures, such as cardiac catheterization and angiocardiology. A classification of congenital cardiac anomalies into four groups, based on changes in the lesser circulation demonstrable in a conventional roentgenogram of the thorax, is proposed. Further subdivisions are based on certain other differentiating features.

CLASSIFICATION OF IMPORTANT CONGENITAL HEART LESIONS

- Increased pulmonary arterial vascularity (increased flow)
 - Ventricular septal defect
 - Atrial septal defect
 - Patent ductus arteriosus
 - Persistent common atrioventricular canal
 - Anomalous pulmonary venous connection
 - Aortopulmonary window
 - Transposition of great vessels*
 - Truncus arteriosus*
- Decreased pulmonary arterial vascularity (decreased flow)
 - Tetralogy of Fallot
 - Pulmonary stenosis with intact ventricular septum
 - Tricuspid atresia
 - Ebstein's malformation
 - Pseudotruncus arteriosus
 - Agnesis of a main branch of pulmonary artery
- Normal pulmonary arterial vascularity (normal flow)
 - Coarctation of aorta
 - Congenital aortic stenosis
- Pulmonary venous hypertension (obstruction to pulmonary venous flow)
 - Left heart failure from any cause
 - Congenital mitral stenosis
 - Congenital stenosis of pulmonary veins

* Increased pulmonary vascularity but with flat or concave pulmonary-artery segment.

A series of roentgenograms illustrates the value of the classification.

WILLIAM MARTEL, M.D.
University of Michigan

Localization of Bullets and Metallic Fragments in the Cardiovascular System: Role of Angiocardiology in 7 Cases. Israel Steinberg. Am. J. Roentgenol. 83: 998-1010, June 1960. (525 E. 68th St., New York 21, N. Y.)

The author reports 7 cases in which bullets and metallic foreign bodies in the cardiovascular system were accurately localized by angiocardiology. Practically all the clinical features produced by foreign bodies in the cardiovascular system were encountered in these cases. Four patients were asymptomatic.

In 2 of the patients, frontal and lateral views demonstrated that bullets were embedded in innocuous parts of the heart (the base of the ventricular septum and undersurface of the right pulmonary artery). In 2 others, although the fragments appeared to be freely movable (aorta, right atrium, and pulmonary veins), their small size made removal undesirable; 1 of these patients became asymptomatic after reassurance, and a cardiac neurosis was prevented. One patient with a large bullet in the left ventricle and with cerebrovascular and cardiac complications was denied operation because the initial injury was believed to be responsible for the progressive disability. Finally, angiocardiology established that the bullets were free in the right atrial appendage in 1 patient and in the inflow tract of the right ventricle in another; removal of the bullet in each instance was curative.

Roentgenography has long been considered essential in the diagnosis and management of bullet wounds and shell fragments. In cardiovascular injuries particularly, roentgen examination has not only revealed metallic objects but has become the most important means of detecting the enlarging and poorly pulsating cardiac silhouette (cardiac tamponade) due to pericardial hemorrhage. Conventional roentgenography, however, cannot accurately localize foreign bodies in the cardiovascular system. The value of angiocardiology for this purpose has been reviewed by Swan *et al.* (Ann. Surg. 135: 314, 1952. Abst. in Radiology 60: 121, 1953).

ROBERT H. LEAMING, M.D.
Memorial Center, New York

The Transverse Diameter of the Heart in Older People. Nairn R. Cowan. Brit. Heart J. 22: 391-394, June 1960. (Consultative Health Centre for Older People, Rutherglen, Lanarkshire, Scotland)

Measurements of the transverse diameter of the heart, as determined from chest films, in persons aged sixty to seventy-nine years, are presented together with body weight, height, chest diameter, and arterial blood pressure. The data were derived from the records of 111 men and 160 women, aged sixty to sixty-nine years, and 123 men and 129 women, aged seventy to seventy-nine years. All were considered to be in good health. The transverse diameters of the heart and chest were measured to the nearest millimeter from roentgenograms taken in the postero-anterior position at a distance of 2 meters.

In this series the average heart diameter differed little in men and women. Body weight and arterial blood pressure were more variable attributes. The transverse cardiac diameter was significantly related to each of the variables mentioned, but most appreciably to body weight and to the transverse diameter of the chest. Equations predicting heart diameter in terms of these two factors are therefore quite as efficient as those using all four variables, and are as follows:

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*Sixty to Sixty-nine Years*Men. $\bar{X}_1 = 0.02571 x_2 + 0.2433 x_3 + 1.9944$ Women. $\bar{X}_1 = 0.01890 x_2 + 0.2245 x_3 + 4.2778$ *Seventy to Seventy-nine Years*Men. $\bar{X}_1 = 0.01656 x_2 + 0.2142 x_3 + 4.6581$ Women. $\bar{X}_1 = 0.01232 x_2 + 0.1951 x_3 + 6.1876$

Where \bar{X}_1 = transverse diameter of heart (cm.), x_2 = weight (lb.), and x_3 = transverse diameter of chest (cm.).

Two tables.

ZAC F. ENDRESS, M.D.
Bloomfield Hills, Mich.

Myxoma of the Left Atrium. Harold E. Aldridge and William F. Greenwood. *Brit. Heart J.* 22: 189-200, April 1960. (Toronto General Hospital, Toronto, Ont., Canada.)

From 1951 to April 1958, some 600 operations for relief of mitral stenosis were performed in the Toronto General Hospital. Three patients believed to have mitral stenosis and advised to undergo commissurotomy were found at operation to have a myxoma of the left atrium. The authors have reviewed 35 cases of left atrial myxoma, including these 3, to see if it is possible to distinguish between mitral stenosis and myxoma of the heart by means other than angiocardiology.

Approximately 75 per cent of myxomas occur in the left atrium; almost all the remainder are found in the right atrium. All arise from a pedicle at the rim of the fossa ovalis. The myocardium is not involved, which may explain why arrhythmias, so common in mitral stenosis, are unusual in myxoma. Eighty per cent of the tumors are polypoid or, occasionally, villous. They are usually soft and extremely friable, and tumor emboli are common.

Thirty of the 35 patients in the series reviewed were thirty years of age or over, and nearly three-fourths were females. Age and sex, therefore, do not help to distinguish myxoma from mitral stenosis. Nor is the history of rheumatic fever or its absence a differential feature. Patients with a history of rheumatic fever have been found to have a myxoma, and myxoma and mitral stenosis have been observed in the same patient. Only about 55 to 60 per cent of the authors' patients with mitral stenosis had had rheumatic fever. The duration of cardiac symptoms is of more significance. In 14 of the 31 patients with myxoma who underwent cardiac surgery, the duration of symptoms was three years or less in 10 and four years or more in 4. Of the 17 patients not subjected to surgery, 14 lived only one year after onset of symptoms and only 2 lived four years or more; remission of symptoms was unusual. In mitral stenosis, on the other hand, 50 per cent of badly disabled patients will live five years. Syncope caused by mitral stenosis is extremely rare, but about 1 in 10 patients with myxoma displays this symptom; its occurrence with signs of mitral obstruction should suggest a tumor. Emboli are common in both myxoma and mitral stenosis.

In 27 of the 35 cases of myxoma, the cardiac sounds were commented on; a loud mitral first and pulmonary second sound were heard in 21, while in a further 3 the pulmonary second sound only was loud. Heart murmurs in patients with myxoma have been said to vary with change in position and from day to day. The diastolic murmur in tight mitral stenosis may be absent or difficult to hear or may be heard only from time to time. Only mitral murmurs were mentioned in 31 of 34 cases of myxoma (details not recorded in 1 case);

25 patients had constant diastolic murmurs. Three patients had no murmurs.

Fluoroscopic or roentgenographic findings were given in 16 cases, consisting in minimal to moderate left atrial enlargement. Some right ventricular enlargement was seen in 9 instances. A further 5 were reported to have enlargement of the pulmonary conus or straightening of the left cardiac border, suggestive of a mitral configuration. Right catheterization was performed in 8 patients; the findings were the same as in mitral obstruction. Angiocardiography was carried out in 5 cases and in each instance a filling defect of the left atrium was demonstrated. In 24 of the 35 cases, the mitral valve was examined at operation or at autopsy; in 21, it was normal.

From their analysis the authors conclude that the differentiation between left atrial myxoma and mitral stenosis is usually impossible by clinical means. When a patient has signs of mitral valve obstruction with a rapid, unremitting downhill course or with syncope, however, angiocardiography should be performed to exclude myxoma. Since the tumor is so rare, routine preoperative angiocardiography in patients suspected of having mitral stenosis is not indicated.

The authors' 3 cases are reported in detail.

Six figures; 4 tables.

WENDELL M. BURNS, M.D.
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"Snowman" Heart. Manifestation of Total Anomalous Pulmonary Venous Connection. Richard L. Golden and Charles A. Bertrand. *J. A. M. A.* 173: 1102-1105, July 9, 1960. (102-40 67th Dr., Forest Hills, L. I., N. Y.)

Total anomalous pulmonary connection is a rare congenital anomaly in which all of the pulmonary veins enter the right atrium or its tributaries. In most instances the pulmonary veins converge at the level of the left atrium and empty into the right heart through a single anomalous vein arising from this confluence. The net effect of this abnormality is the recirculation of blood in the lesser circulation, an increased work load on the right heart, and deprivation of the systemic circulation of its normal share of oxygenated blood. The authors report an unusual case of this anomaly and stress the importance of early diagnosis by means of the "snowman" cardiac configuration, demonstrable on routine films.

A 16-year-old boy was admitted to the hospital for evaluation of his cardiac status. A diagnosis of congenital heart disease had been made at the age of six months. Cyanosis, in the form of "blueness of the lips," together with shortness of breath, was first noted after strenuous activity at seven years. Growth was mildly retarded, hemoglobin values were slightly increased, and a harsh Grade III systolic murmur was heard over the precordium. An electrocardiogram suggested enlargement of the right atrium and right ventricular hypertrophy. Roentgen examination of the chest showed increased pulmonary vascularization and evidence of hypertrophy of the right ventricle. The most striking finding was the "snowman" configuration of the heart in the frontal projection [compare with the term "figure-8" heart used by other authors for this feature—J. W. B.] A diagnosis was made of complete anomalous pulmonary venous connection *via* the left and right superior venae cavae and of atrial septal defect.

The findings in the authors' case were similar to those in other examples of this anomaly recorded in the literature. The authors state that, although many patients die in infancy and childhood, the development of new surgical techniques, with use of extracorporeal circulation and hypothermia, has permitted the successful correction of the disorder in some instances.

One roentgenogram; 1 electrocardiogram.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Percussion of the Sternum. I. Aid to Differentiation of Pericardial Effusion and Cardiac Dilatation. William Dressler. *J. A. M. A.* 173: 761-764, June 18, 1960. (1150 5th Ave., New York 28, N. Y.)

Thirty-two cases of pericardial effusion were studied, and a comparison was made of the accuracy of the single chest roentgenogram and sternal percussion as a means of diagnosis. Pericardial effusion was diagnosed correctly from a single roentgenogram in 13 per cent (4 of 32 cases), while percussion yielded the correct diagnosis in 58 per cent (in 17 of the 29 cases in which adequate records were available). A flat percussion note over the lower half of the sternum, sometimes extending upward as far as the level of the second costal cartilage, proved to be the most reliable sign in the diagnosis of pericardial effusion. Two other large areas of flat percussion sound were often observed, one in the left third intercostal space adjacent to the sternum and the other extending from the sternum to the right side between the third and sixth ribs. The procedure of percussion can be simplified by fixing attention on areas of flat percussion sounds and disregarding intermediate degrees of dullness.

Two roentgenograms; 1 drawing.

WILLIAM MARTEL, M.D.
University of Michigan

Mild Pulmonic Stenosis: A Clinical and Hemodynamic Study of Eleven Cases. Stephen M. Ayres and Daniel S. Lukas. *Ann. Int. Med.* 52: 1076-1087, May 1960. (D. S. L., 525 East 68th St., New York 21, N. Y.)

With recent widespread use of cardiac catheterization as a diagnostic tool, it has become increasingly apparent that isolated pulmonic stenosis, uncomplicated by defects of the septum, is a relatively common congenital anomaly. The clinical spectrum of pulmonic stenosis ranges from very mild to very severe. The serious nature of the anomaly has been stressed in the literature, and only recently have the milder cases received any attention. This may be due partially to the difficulty of their diagnosis by clinical means alone, since the signs and symptoms diverge in several respects from the classical clinical pattern of the disease. The authors review the clinical manifestations in 11 patients in whom the diagnosis of mild isolated pulmonic stenosis was established by cardiac catheterization.

The patients ranged in age from thirteen to fifty-four years. Seven were males and 4 females. Nine were completely asymptomatic; 2 experienced some dyspnea and fatigue. A systolic murmur of varying intensity and quality was present over the pulmonic area in all, and 4 had a short blowing diastolic murmur along the left sternal border. A systolic click was noted in the pulmonic area in 4 patients.

The most striking abnormality on fluoroscopy and conventional roentgenography was the enlargement of

the main pulmonary artery; this was usually of considerable degree and in 1 instance was of aneurysmal proportions. Pulsations in the artery and its branches were of normal amplitude, and vascularity of the lung fields were unremarkable. Size and configuration of the heart was unremarkable except for slight prominence of the right ventricle in 1 patient. Fluoroscopically, the right ventricle appeared to be slightly enlarged in 3 others. Angiocardiography, performed on 6 patients, revealed the enlargement of the pulmonary artery to be confined to the main stem and, occasionally, the left branch. Characteristically, the main artery was ballooned out superiorly but of normal diameter at the valve ring, thus giving the appearance of an inverted pear. In no instance was chamber enlargement demonstrated.

Two patients had suggestive electrocardiographic evidence of right ventricular hypertrophy. One had a complete right bundle branch block; 2 others, an incomplete right bundle branch block.

The mildness of the lesion is indicated by the levels of the resting right ventricular systolic pressure, which were below 40 mm. Hg in 9 instances. The peak systolic pressure gradient across the pulmonic valve in 10 of the patients ranged from 7 to 20 mm. Hg, indicating that from 23 to 54 per cent of the right ventricular systolic pressure was dissipated in forcing blood through the stenotic valve orifice. Cardiac outputs and arterial oxyhemoglobin saturations were normal. There was no evidence of intracardiac shunts.

Clinically, the lesion was commonly confused with patent ductus arteriosus and ventricular septal defect.

Four roentgenograms; 1 phonocardiographic and electrocardiographic tracing; 2 tables.

STEPHEN N. TAGER, M.D.
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Roentgenologic Diagnosis of Congenitally Corrected Transposition of the Great Vessels. Richard G. Lester, Ray C. Anderson, Kurt Amplatz, and Paul Adams. *Am. J. Roentgenol.* 83: 985-997, June 1960. (University of Minnesota Hospitals, Minneapolis 14, Minn.)

Congenitally corrected transposition of the great vessels is a malformation in which the pulmonary artery and the aorta are transposed in relation to each other but in which the flow of blood is maintained in the physiologic direction. There is a concomitant inversion of the ventricular chambers. The anomaly is important because it is usually associated with other defects, many of which can be corrected surgically. The condition was first recognized in 1875 (von Rokitsansky) and until recently was considered exceedingly rare.

Forty of 60 cases of congenitally corrected transposition of the great vessels seen in the Variety Club Heart Hospital of the University of Minnesota have been reviewed with special attention to the roentgen features. All of the patients had other congenital cardiac defects as well, the most common being interventricular septal defect, single ventricle, and tetralogy of Fallot. There were 22 males and 18 females in the series; the age range was from three months to forty-four years.

The existence of the abnormality may be suspected on the basis of conventional roentgenograms. The upper left border of the cardiac silhouette in the frontal view is made up by the ascending aorta. Consequently, a single gentle convexity is frequently seen in this area in place of the normal double convexity of the aortic arch

and the undivided pulmonary artery. The left heart border then shows but two convexities instead of the normal three. In other cases the upper left border of the heart silhouette may be gently concave instead of convex, even in the presence of a left-to-right shunt. The pulmonary artery is medially placed and usually, but not invariably, is not a part of the left border of the heart. It may cause a distinct impression upon the esophagus below the area of the normal indentation of the arch of the aorta.

During cardiac catheterization, if both the pulmonary artery and the aorta can be entered, a definitive diagnosis of congenitally corrected transposition can be made. When the pulmonary artery can be entered but the aorta cannot, the evidence is highly suggestive but not always definitive.

The diagnosis of congenitally corrected transposition is most firmly established by angiocardiology. In the 32 cases in the present series in which this procedure was performed, the angiocardiology was diagnostic. It is crucial to remember that the most important features are best seen in the frontal plane. Once again, the position of the undivided pulmonary artery and of the aorta is of utmost value. The pulmonary artery is seen medially and the ascending aorta to the left laterally. The pulmonary valve is depressed and lower than the aortic valve. In the frontal view frequently, but not invariably, the pulmonary pumping ventricle, which is situated anteriorly, presents a tail-like projection toward the apex of the heart with the chamber having an almost triangular shape. The absence of an infundibulum for this ventricle can be appreciated from a study of the angiocardiology. In consequence, pulmonary stenosis is seen invariably to be of valvular or subvalvular type. The pulmonary stenosis of tetralogy of Fallot associated with congenitally corrected transposition is also of this type.

It is hoped that an awareness of this condition on the part of the radiologist will lead to its more frequent demonstration as an isolated anomaly.

Twenty-seven roentgenograms; 2 diagrams; 1 table.

ROBERT H. LEAMING, M.D.
Memorial Center, New York

Traumatic Aneurysm of the Thoracic Aorta. R. S. MacIntyre. *Am. J. Roentgenol.* **83**: 1011-1019, June 1960. (Hermann Professional Bldg., Houston 25, Texas)

A review of 100 cases of thoracic aortic aneurysm of various types, referred to the Methodist Hospital, Houston (Texas), disclosed 8 verified cases of traumatic aneurysm which were characteristic in appearance and location. In each of these there was a history of severe trauma that included injury to the chest with recognized or unrecognized injury to the aorta. The intrathoracic abnormality was detected weeks, months, or even years after the original injury. Syphilis, atherosclerosis, and other causes for the aneurysm could readily be excluded in the type of patient under discussion. None had significant hypertension; only 1 was over fifty years of age.

The most common site of traumatic rupture of the aorta is just beyond the origin of the left subclavian artery; rupture above the aortic cusps and at the level of the diaphragm occurs less often. Anatomic fixation of the aorta at these sites, with relative freedom of motion of adjacent parts, seems a reasonable explanation for the frequency of rupture at these levels.

Roentgenographically none of the patients showed any evidence of change in the aorta other than a localized abnormal process. In each case calcification was demonstrable.

Traumatic aneurysm of the thoracic aorta should be suspected on routine roentgen examination by (1) its location distal to the left subclavian artery near the junction of the arch and descending portion; (2) calcification in the wall (late cases); (3) evidence of previous trauma to the thoracic cage; (4) age of the patient, without other evidence of vascular disease; and (5) absence of positive serologic findings in a non-motensive person.

Eighteen roentgenograms. PAUL MASSIK, M.D.
Quincy, Mass.

Intravenous Aortography. Technique and Clinical Aspects. Richard H. Greenspan, Eugene F. Bernstein, and Merle K. Loken. *Am. J. Roentgenol.* **83**: 1034-1041, June 1960. (Yale University School of Medicine, New Haven 5, Conn.)

Because the use of the translumbar route for aortography entails a considerable risk, the authors have developed a venous method. Basically, intravenous aortography depends on obtaining properly timed roentgenographic exposures of the aorta following the rapid intravenous injection of a large amount of concentrated opaque material.

Predetermination of the vein-to-aorta circulation time establishes the interval between venous injection and aortic opacification. For this purpose, a No. 280 polyethylene catheter is inserted into the median antecubital vein under local anesthesia and advanced 3 or 4 inches up the arm. Fifty microcuries of I^{131} -labeled Renografin, 2 c.c. of stable Renografin 76 per cent, and between 60 and 75 c.c. of saline are then injected rapidly into the catheter. A collimated scintillation counter is held over the abdominal aorta or over that vessel which is to be examined roentgenographically, and impulses are recorded by an Esterline Angus recorder. Arm vein-to-abdominal aorta circulation time is thus obtained. In the interests of accuracy it is necessary to use a volume of material approximating that of the main injection. If a small volume (2 to 5 c.c.) is injected, the circulation time may be as much as five seconds slower than with the larger amount.

The contrast material, consisting of between 65 and 100 c.c. of 85 or 90 per cent diatrizoate, is then injected into the catheter as rapidly as possible. Following a pause equal to the vein-to-aorta circulation time, as previously determined, roentgenograms of the abdomen are taken in either one or two planes. In the majority of the authors' studies, a Schönander biplane apparatus was employed, with one exposure per second for approximately eight seconds. In cases in which delineation of the femoral vessels is desired, a single long exposure is made at low milliamperage.

Forty-six thoracic and 158 abdominal aortographic examinations have been performed with the intravenous technic. Adequate concentration of opaque material for diagnostic visualization of the aorta was obtained in all of the thoracic and in 91 of the abdominal cases. [There is some discrepancy in the authors' figures here. The text reads "91 (91 per cent)," so that the results would appear to be based on only 100 cases instead of 158.—Ed.] In 5 instances failure of visualization was due to mechanical malfunction of the rapid cassette changing apparatus. In 4 the technic was adequate,

but the concentration of contrast medium in the abdominal aorta was insufficient for diagnostic purposes.

Intravenous aortography has proved most useful in the pre- and postoperative evaluation of patients with suspected or known abdominal aortic aneurysms. It yields valuable information as to the extent of the aneurysm and the condition of the bifurcation of the aorta. It will also reveal the presence or absence of renal artery involvement and may indicate the existence of multiple aneurysms when only one was suspected clinically. Additional intravenous aortograms may be of value in the postoperative period following aortic grafting procedures. Occlusion of the aorta, the iliac, and the femoral arteries is also well demonstrated. There have been no serious complications or deaths associated with the procedure.

Twelve roentgenograms. PAUL MASSIK, M.D.
Quincy, Mass.

Radiological Appearances of Pulmonary Hypertension. J. K. McMyn. J. Coll. Radiologists Australasia 4: 21-28, June 1960. (Green Lane Hospital, Auckland, N. Z.)

It is important to differentiate between pulmonary arterial hypertension and pulmonary venous hypertension. The differences between these two types of pulmonary hypertension have been discussed fully by Goodwin *et al.* (Brit. J. Radiol. 31: 174, 1958. Abstr. in Radiology 72: 293, 1959). Increased resistance in the pulmonary arterioles will obviously produce a rise in pulmonary artery pressure, but not in pulmonary venous or left atrial pressures; this the above authors call precapillary resistance. On the other hand, back pressure (postcapillary resistance) due to mitral stenosis or left ventricular failure may produce a rise in venous and left atrial pressures. Septal lines (Kerley's B lines) are a sign of venous hypertension and are due to interstitial pulmonary edema or edema of the interlobular septa. They are sharply defined, whereas vessels are slightly blurred or irregular.

Fifty-six cases of mitral stenosis were investigated by the author and an attempt was made to correlate certain roentgen changes, such as (1) the presence of septal lines in the lung fields and (2) the size of the main pulmonary artery and its branches, with the pulmonary venous and pulmonary arterial systolic pressures.

All cases showing well marked septal lines had pulmonary venous pressures of over 20 mm. Hg. The critical pressure appears to be between 17 and 25 mm. The presence of septal lines in a patient with mitral disease suggests the presence of a tight mitral stenosis.

There was no close relationship between septal lines and pulmonary arterial pressure, though the presence of septal lines was found to indicate a pulmonary arterial systolic pressure of over 30 mm. Hg, the normal being 20 to 25 mm. The absence of septal lines, however, does not exclude pulmonary arteriolar hypertension in mitral disease.

The size of the main pulmonary artery as shown on a postero-anterior view of the chest correlated well with pulmonary artery systolic pressure. All cases with any prominence of the pulmonary artery had pressures of over 30 mm. Hg. As demonstrated by Goodwin *et al.*, in cases of well developed pulmonary arteriolar hypertension there is peripheral constriction of the lung fields.

As expected, the size of the pulmonary artery correlated poorly with pulmonary venous hypertension.

It is noted that in pure pulmonary arteriolar hypertension, as in congenital heart disease or in primary pulmonary hypertension, the pulmonary venous pressure approaches the normal.

Eight roentgenograms; 5 diagrams.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Collateral Circulations in Obstructive Syndromes of the Superior Vena Cava and Its Larger Branches. G. F. Garusi. Radiol. clin. 29: 148-168, June 1960. (In English) (Istituto del Radio, Policlinico S. Orsola, Bologna, Italy)

The superior and inferior venae cavae represent the two main channels of venous flow toward the right cardiac cavity; they collect the blood flowing from the superior and inferior halves of the body. The communications between these two networks include the system of the azygos veins, internal mammary veins, lateral thoracic veins, and the vertebral venous plexuses. Through these venous networks, collateral or compensatory circulations are established in the case of obstructive syndromes of the superior vena cava and its larger branches. An adequately performed phlebography is the best radiologic method for ascertaining the distribution and entity of these collateral circulations.

Eight case reports are presented with good roentgenographic reproductions. The chief causes of compression are malignant tumors, benign tumors, sclerotic processes due to scar formation, and diseases of the cardiovascular system. Malignant tumors include those of the lung and pleura, mediastinal lymph nodes, esophagus, thyroid, and thymus, as well as metastatic neoplasms. Benign tumors are adenoma of the thyroid, cystic formations, fibromas, and lymphangiomas. Sclerosis may be due to chronic inflammatory processes as mediastinitis, adenopathies, abscesses, tuberculosis, silicosis, and syphilis, or may be reactive, following operation, trauma, or irradiation. Diseases of the cardiovascular system producing vena caval obstruction include tricuspid valvular disease, mitral-tricuspid valve disease (in failure), aneurysms of the aorta and its principal branches, constrictive pericarditis, and peripheral thrombosis.

Angiographic studies have shown a certain variability in the distribution and type of compensatory circulation in vena caval obstruction, the understanding of which is a great aid in diagnosis, prognosis, and therapy.

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Some Aspects of Cine- and High Speed Serial Angiographic Techniques. Theodore E. Keats, Gwilym S. Lodwick, and George F. Koenig. Am. J. Roentgenol. 83: 1067-1077, June 1960. (University of Missouri School of Medicine, Columbia, Mo.)

Although angiocardiology is now a well accepted diagnostic procedure, there exists considerable difference of opinion concerning the best technic for recording the roentgen data, some advocates of angiocardiology preferring cinerentgenography and others high-speed serialography. The authors describe an investigation directed toward three broad aspects of the problem relating to these two modalities: (1) dosimetry; (2) relative diagnostic effectiveness; (3) evaluation of the relative roentgen opacities of various concentrations of contrast media.

Dosimetry: In both cine- and serial angiocardioraphy, the hazard of excessive radiation is very real, particularly since most of the patients have already received considerable fluoroscopic and roentgenographic exposure. Direct radiation measurements were made utilizing a phantom constructed with a human skeleton without extremities. Surface radiation doses were recorded with a Victoreen Model 70 condenser r-meter with 1- and 5-r chambers. Gonadal doses and doses to personnel were recorded with Victoreen pocket dosimeters, Model 362, which have a range of 0 to 0.2 r.

It was found that there is not a remarkable difference in dose to the exposed skin with the two technics. It must be borne in mind, however, that the area irradiated in the cinerentgenographic examination was much smaller than with serial roentgenography. With the use of 8- or 11-inch amplifiers, the dose may well exceed that obtained in serial roentgenography by a significant degree.

With small-field cinerentgenography, scatter to the gonads is not a significant problem. In fact, even with the large fields of serial roentgenography, the amounts which reach the gonads are very small. Scatter to the gonads is primarily through tissue rather than through air. For this reason, external shielding would probably add very little protection. Proper collimation of the beam, however, is of the utmost importance in gonadal protection against direct and scattered irradiation.

With cinerentgenography the radiation hazard to attendant personnel is solved by the rubber apron attached to the fluoroscope. Even in serial roentgenography, however, the amount of scattered radiation is surprisingly small. The safest position for an attendant would appear to be at the head of the patient. A position lateral to the thorax should be avoided. In all instances, protection of personnel apparently can be easily handled by proper shielding by barricades.

Relative Diagnostic Effectiveness: The question of the relative diagnostic effectiveness of serial and cineangiocardioraphy is a matter of practical importance. Four anatomic entities were studied in 4 dogs with both methods: the normal pulmonary and aortic valves, experimentally produced atrial septal defect, experimentally produced ventricular septal defect, and coronary arteries. In those lesions where the dynamics of flow are important, particularly in the shunts, cineangiocardioraphy proved to have real diagnostic advantages. In entities where a study of detailed structure is important, e.g., where the details of valve leaflets or the coronary arteries are to be demonstrated, the serial roentgenographic examination appears to yield more information. With study of individual films or frames, the superiority of detail of the serialographic film is beyond question.

Relative Roentgen Opacities of Contrast Media: Accumulated experience in angiocardioraphy suggests that there is a significant relationship between complications or death and the volume and concentration of the contrast material employed. Experimental testing by the authors indicates that the radiopacity of 50 per cent and 85 per cent Hypaque is strikingly similar and that the advantages of the additional opacity of the more concentrated medium are largely offset by the disadvantages of its inherent increased viscosity and toxicity.

Ten roentgenograms; 2 charts; 1 drawing; 6 tables.

NORMAN L. ARNETT, M.D.
Anaheim, Calif.

Experiences with Angiography as a Guide to Mediastinal Exploration. Owings W. Kincaid, Robert O. Brandenburg, and Philip E. Bernatz. J. A. M. A. 173: 613-624, June 11, 1960. (The Mayo Clinic, Rochester, Minn.)

Angiocardioraphy and thoracic aortography have been performed at the Mayo Clinic in 200 patients with a variety of mediastinal lesions. The authors describe briefly the technics employed in this series and report 12 cases selected to illustrate the value of the procedures. Angiography has proved a safe and highly accurate method of distinguishing vascular from nonvascular diseases without thoracotomy, and of determining the exact nature, extent, and probable resectability of all vascular lesions of the mediastinum. The latter consideration is of increasing importance in view of the recent advances made in the field of vascular surgery. In many instances it is possible to avoid unnecessary and possibly hazardous mediastinal surgery, and in others the necessity of surgical exploration is clearly indicated and intelligent surgical planning is made possible. While simple chest roentgenograms and fluoroscopy are highly accurate in detecting the presence of mediastinal lesions, the findings frequently are not specific enough to permit determination of the exact nature and extent of lesions so revealed.

Thirty-four roentgenograms.

WILLIAM MARTEL, M.D.
University of Michigan

Potassium Iodide Screens and High Capacity Roentgen Tubes in Angiocardioraphy. Erik Carlsson. Acta radiol. 53: 481-485, June 1960. (Washington University School of Medicine, St. Louis, Mo.)

An investigation carried out by the author showed that thallium-activated potassium iodide intensifying screens in combination with high-capacity roentgen tubes produce the optimal energy level for angiocardioraphic examinations. They allow reductions in the concentration of iodinated contrast media required for satisfactory density, thereby decreasing the risk of reaction and of the dose of radiation. These advantages are to some extent offset by the drawback of mottling of the films with the experimental screens and by the geometrical unsharpness caused by the large focal spot of high-capacity roentgen tubes. It is expected that the first disadvantage may be overcome somewhat by the use of refined commercial screens.

Two roentgenograms; 1 diagram.

Arteriographic Demonstration of Stationary Arterial Waves. Georg Theander. Acta radiol. 53: 417-425, June 1960. (Malmö Allmänna Sjukhus, Malmö, Sweden)

Occasionally, during arteriography, a characteristically regular change in the width of segments of apparently normal vessels occurs, giving an appearance resembling a string of pearls. The author proposes that the descriptive term "stationary arterial waves" be applied to this phenomenon. In an investigation of these waves, the films from 217 consecutive arteriographic examinations of the lower limb, performed in 160 patients, were reviewed. A standard technic was employed in the examinations, using 30 c.c. of 60 per cent Urografin and direct femoral puncture.

The stationary arterial waves were observed in 4 patients. All were under sixty, although 79 of the 160

patients in the series were over that age. In 3 of the 4 cases, the phenomenon proved to be transitory. In all cases the waves were situated proximal to a vascular region in which arteriographic or microscopic examination revealed lesions capable of interfering with the flow of the blood and contrast medium. Two patients suffered from arterial embolism, 1 had clinical and arteriographic signs of thrombo-angiitis obliterans, and 1 had vascular lesions of obscure origin. The waves did not occur in extremities with many wide collaterals. Their size appeared to depend on the width of the vessel involved.

Previously, these stationary arterial waves have been attributed to "arterial spasm" (see, for example, Lindbom: *Acta radiol.* **47**: 449, 1957. *Abst. in Radiology* **70**: 613, 1958). This view is not supported by the fact that in the present series there was obvious widening of vessel segments when stationary arterial waves were seen. The author believes that these waves are standing waves amplified by resonance, a pressure-induced phenomenon when flow is partially arrested. This would explain the hitherto known properties of arterial waves, e.g., their rarity and transiency, their relation to age and disease, their location proximal to vascular lesions, their effect on the width of the lumen, as well as the relation of their size to vessel caliber.

Eleven roentgenograms; 2 diagrams.

CAPT. JOHN R. BROADWATER, M.C.
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Serial Femoral Arteriography in Occlusive Disease. Clinical-Roentgenologic Considerations with a New Classification of Occlusive Patterns. Henry Haimovici, Jerome H. Shapiro, and Harold G. Jacobson. *Am. J. Roentgenol.* **83**: 1042-1062, June 1960. (Montefiore Hospital, New York 67, N. Y.)

In femoral arteriography, an evaluation of the site and extent of segmental occlusion, the state of the distal arterial tree, and the degree of collateral circulation can best be obtained by serialographic studies. The authors describe their technic of serial femoral arteriography with emphasis on its advantages, present a classification of the arteriographic patterns of occlusive arterial disease based on a survey of unselected patients, and interpret and evaluate the significance of these various patterns.

Full-length multifilm visualization is best secured by an automatic long-segment serialograph. All femoral arteriographies were performed by the percutaneous route. In the early part of the series, the contrast medium employed was 35 per cent iodopyracet (Diodrast); later 50 per cent sodium diatrizoate (Hypaque) was used in the majority of cases. An intravenous or intra-arterial sensitivity test was performed before each examination, and no significant allergic reactions were encountered.

The study is based on 102 consecutive femoral arteriograms of 91 patients. The age range was from twenty-nine to eighty-seven years, with the majority of patients in the sixth and seventh decades. There were 64 men and 27 women. The presenting clinical manifestations were: intermittent claudication alone in 33 per cent; rest pain without trophic lesions in 22 per cent; rest pain associated with ulcers of the foot or leg in 17 per cent; gangrene in 28 per cent.

In order to facilitate an evaluation of the occlusive disease in the femoral-popliteal segment, a classification was adopted based upon the location and extent

of the occlusion. Nine patterns emerged from this classification. The total combined incidence of the first 3 patterns (femoral occlusion) was 36.4 per cent and that of the next three patterns (popliteal occlusion) was 32.7 per cent. This slight difference is at variance with the much higher incidence of femoral artery occlusion commonly accepted. The difference may be due to the high percentage of patients with diabetes and advanced arterial disease in the present series.

The seventh pattern, occlusion of the entire superficial femoral and the entire femoral-popliteal segment, was more often seen in arteriosclerotic nondiabetic patients than in diabetics. Occlusion of the profunda femoris artery (pattern 8) was surprisingly high, with a preponderance in diabetic patients. In 12.7 per cent of the series diffuse atherosclerosis with no occlusion (pattern 9) was demonstrated.

The "run-off" represents the patent major distal vessel below the site of segmental occlusion. This vascular channel is fed by a number of collaterals. The presence of an adequate outflow or "run-off" is the most decisive factor in the selection of patients for arterial grafting or thrombo-endarterectomy. Patients having a complete block of the distal popliteal artery and its bifurcation are generally not suitable for such procedures. Evaluation of the "run-off" was done only in patients displaying an open distal popliteal artery and its bifurcation. One-half of the cases in this series met this condition. In this group, 33 were arteriosclerotic nondiabetics and 18 arteriosclerotic diabetics. The "run-off" was graded as good, fair, or poor, according to the degree of atherosclerotic involvement of the major distal vessel. A good "run-off" was about three times as frequent in the arteriosclerotic nondiabetic patients as in the diabetics; conversely, a poor "run-off" was twice as frequent in the diabetics as in the nondiabetics.

Good visualization of the leg arteries was obtained in 86 of the 102 femoral arteriograms. In 70, there was seen an associated involvement of the femoral-popliteal segment, and in 3 instances the distal popliteal artery was blocked. In the remaining 13, the leg arteries alone were the site of the occlusive process, although the femoral-popliteal segment displayed diffuse atherosclerosis. From the data obtained, it appears clear that the incidence of involvement of the leg arteries is much higher in diabetics than in nondiabetics.

Comparison of the degree of "run-off" with that of the collaterals indicates a good correlation between these two components in arteriosclerosis obliterans and an inverse relationship in arteriosclerosis with diabetes.

By far the most common form of calcification encountered was that of the intimal type. Roentgenograms failed to show any degree of calcification in 38.5 per cent of the arteriosclerotic patients and in 13.8 per cent of the diabetic patients. In contrast, moderate to marked calcification was found in 42 per cent of the diabetics as compared with 26 per cent of the nondiabetics.

Prognosis for an extremity with occlusive arterial disease depends on many factors, both general and local. Of the general factors, diabetes plays a predominant role. Infection, when present, is a serious complication. Of the local factors, the pattern of occlusion and the degree of compensatory collateral circulation are decisive. It is generally difficult to assess the prognosis in a given occlusion pattern. However, the overall clinical and arteriographic correlation shows that

prognosis in superficial femoral artery occlusion is much better than in popliteal artery occlusion. A combination of two or more occlusion patterns, particularly if the popliteal artery is involved, further aggravates the prognosis. Furthermore, occlusion of leg arteries associated with any occlusion pattern of the femoral-popliteal segment will materially reduce the terminal arterial flow and thus will lead to gangrene.

Twelve roentgenograms; 4 photographs; 14 drawings; 10 tables.

NORMAN L. ARNETT, M.D.
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Evaluation of Vertebral Venography. M. H. Nathan and Luis Blum. *Am. J. Roentgenol.* **83**: 1027-1033, June 1960. (L. B., Baylor University College of Medicine, Houston, Texas)

The investigation described here was performed to evaluate the usefulness of vertebral venography in the detection of early vertebral metastases, as well as spinal canal tumors, herniation of the nucleus pulposus, and esophageal varices.

Vertebral venography was attempted in 31 patients, in 6 of whom the examination was a complete or partial failure. The successful series included 11 cases of malignant tumor without known metastases, 4 of obvious vertebral metastases, 4 of esophageal varices, 2 of spinal cord tumors (meningiomas), 2 of postoperative spinal defects, 1 herniated nucleus pulposus at L5-S1, and 1 case of congenital heart disease.

The tip of a No. 14 thin-walled needle with a stylet was inserted into the femoral vein percutaneously immediately below the inguinal ligament. A plastic tube was connected to the needle and, with a Robb-Steinberg syringe, 40 c.c. of 70 per cent Urokon was injected manually after abdominal compression had been applied over the inferior vena cava (after examination of the abdomen to exclude aortic aneurysm or other masses which might present serious complications if compressed). A 14 × 17-inch film was exposed immediately after the completion of the injection. When multiple roentgenograms were taken with the Sanchez-Perez cassette changer, the first exposure was made about one-half second before the injection was complete. Whenever possible, lateral as well as antero-posterior views were obtained and the region of the azygos and hemiazygos veins was included in the examination field. An arbitrary limit was set of 80 c.c. of opaque medium in two injections.

Visualization of any of the vertebral system was considered the criterion for a successful examination. The epidural veins were visualized in 21 patients, and the contrast material was demonstrated as far cephalad as T9 or T10 in 16. Only 6 showed filling cephalad to this level. In the 4 patients with far advanced, widespread metastases, there was no evidence of obstruction, compression, displacement, or abnormality of the vertebral veins. In the case of meningioma at T10, revealed by myelography, there was a question as to whether or not the epidural veins were blocked; it is more probable that in this instance the medium had disappeared from the epidural veins at the tumor level because of shunting into the azygos and hemiazygos.

It is thought that vertebral venography has a useful application in the differentiation of mediastinal masses from enlarged azygos veins. The wide normal variation in the size of this latter vessel makes it unlikely that anything less than marked dilatation can be demonstrated; therefore, the employment of vertebral

venography to visualize esophageal varices at any earlier stage than is possible by conventional roentgenographic methods appears to be of questionable value. On occasion, vertebral venography may be indicated in lesions of the spinal cord below the level of T10 when for some reason myelography cannot be performed or when epidural varices are suspected. The examination may also be helpful in the diagnosis of mediastinal or pelvic masses or venous compression. It is considered valueless for the detection of vertebral metastases.

Seven roentgenograms; 1 drawing.

PAUL MASSIK, M.D.
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Experimental Intraocular Venography. Bruce E. Cohan. *Arch. Ophthalm.* **63**: 489-502, March 1960. (National Institutes of Health, Bethesda 14, Md.)

A method of angiography is described which permits visualization of the intraocular venous circulation in the intact eye of a living cat. The anterior ciliary vein is cannulated and then perfused with radiopaque contrast material. Radiographs of the eye during perfusion clearly demonstrate anatomic details of the intrascleral venous plexus, the long posterior ciliary veins, the intrascleral connections, the veins of the vessel layer of the ciliary body, the vortex sinuses and veins, and the choroidal venous circulation. The radiographic evidence fails to confirm the presence of focal changes in the caliber of choroidal veins. Some evidence is given suggesting the existence of a direct connection between anterior chamber and intrascleral veins, communication between these veins and the venous system of the ciliary body, and strangulation of the vortex veins under circumstances of elevated intraocular pressure.

Eleven roentgenograms; 12 drawings; 2 photographs.

AUTHOR'S SUMMARY

Left Ventricular and Systemic Arterial Catheterization: A Simple Percutaneous Method Using a Spring Guide. Charles T. Dotter. *Am. J. Roentgenol.* **83**: 969-984, June 1960. (University of Oregon Medical School, Portland 1, Ore.)

A detailed technical description is presented of the use of a flexible coil spring guide which gives access to the left ventricle, the aorta, and the systemic arteries. The author states that it takes longer to describe the procedure than it often takes to perform it. Briefly, it consists of introducing a needle into the femoral artery and passing a long, flexible spring guide through the needle. The needle is immediately removed and polyethylene tubing is slipped along the guide into the artery. Guide and tubing are advanced until the desired position is achieved, whereupon the guide is withdrawn, leaving the tubing in place to allow contrast or other injections, the removal of blood samples, or the determinations of pressures. The two main features of the method are (1) the *percutaneous* route, and (2) *simple, atraumatic retrograde passage through the aortic valve*.

Under careful supervision, the procedure is about as safe as angiocardiology and, since in cooperative patients local anesthesia suffices, it is suitable for outpatient use. It is more selective, more reliable, and less hazardous than ordinary translumbar aortography. It can be performed in fifteen minutes by a trained operator with adequate technical support.

The author has used the procedure in over 110 patients, with a minimum of complications: (1) A child

with tetralogy of Fallot died of cardiac arrest. (2) An elderly decompensated woman died of ventricular fibrillation which began during a supra-aortic injection; her death was clearly related to the contrast agent and not the method of injection. (3) Transient hemiplegia appeared in a 9-year-old child eight hours after the study; this was not attributed to the procedure itself. The contrast media employed were Urokon Sodium 70 per cent and Ditriakon, a comparatively new agent.

The procedure allows the direct demonstration of congenital and acquired cardiac lesions and is considered by the author to be essential to the preoperative study of candidates for open heart surgery.

Nineteen roentgenograms; 2 photographs; 1 pressure recording; 1 table.

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The Medial and Lateral Choroid Arteries. An Anatomic and Roentgenographic Study. James R. Galloway and Torgny Greitz. *Acta radiol.* 53: 353-366, May 1960. (T. G., Serafimerlasarettet, Stockholm, Sweden)

The finding of an apparent discrepancy between the angiographic changes in the posterior choroid arteries arising from tumors in the pineal region or thalamus and the changes expected from the reported normal anatomy (Namin: *L'angiographie vertébrale*. Rev. in *Radiology* 67: 112, 1956; Löfgren: *Acta radiol.* 50: 108, 1958. Abst. in *Radiology* 72: 771, 1959) led the authors to a systematic investigation of this subject. The anatomy of the posterior choroid arteries was studied by means of anatomic dissection combined with roentgen examination of the specimens. The basilar artery was injected at necropsy in 20 cases, with a gelatin-barium solution after ligation of the posterior communicating arteries.

The authors found the current nomenclature to be inadequate in that the so-called "posterior choroid arteries" had an entirely separate origin and course. One vessel in its entire course was situated medial to the posterior communicating artery, and it is proposed that this vessel be called the "medial choroid artery." Lateral to the posterior cerebral artery within the choroid fissure usually lay two arteries which the authors would call the "lateral choroid arteries." The medial choroid artery runs parallel to the posterior cerebral artery, around and closely adherent to the brain stem; its course, as seen from the lateral aspect, roughly resembles a figure 3. Contrary to the anatomical description of Namin and Löfgren, the lateral choroid arteries have no relationship whatsoever to the course of the medial choroid artery. They do not lie adjacent to the pineal body as does the medial choroid artery and, of course, they do not pass through the inter-ventricular foramen to supply the choroid plexus of the upper part of the lateral ventricle.

The normal anatomy of the choroid arteries was also studied by means of vertebral angiography. The central branches of the posterior cerebral artery, including the choroid arteries, are rarely identifiable in frontal projections, but they can be seen in lateral views. The medial and lateral choroid arteries extend upward in a posteriorly directed convex curve from the posterior cerebral artery. It is actually the posterior lateral choroid artery which is visualized running above the medial choroid in the larger smooth curve as it

passes posterosuperiorly upon the thalamus in the choroid fissure. Thus, the position of the choroid fissure and the size of the posterior part of the thalamus can be determined.

The authors feel that Löfgren's description and measurements do not accurately reflect the growth of expanding lesions in the pineal region until there has been extension laterally into the thalamus, with consequent elevation of the choroid fissure. The earliest arterial change would be a local deformity of the artery adjacent to the pineal body. As the tumor enlarges there may be an element of posterior displacement of the medial choroid artery. In an expanding lesion arising posterior to the pineal body, such as a meningioma from the tentorium, the medial choroid artery is displaced forward, while the lateral choroid arteries remain unchanged. If the tumor arises within or extends into the thalamus, the lateral choroid artery on the side of the tumor will be stretched and displaced in a bow laterally and posterosuperiorly.

Eighteen roentgenograms; 4 photographs; 3 drawings.

JULIAN O. SALIK, M.D.
Baltimore, Md.

Effort Thrombosis of the Subclavian and Axillary Veins: Review of the Literature and Case Report with Two-Year Follow-Up with Venography. David L. Crowell. *Ann. Int. Med.* 52: 1337-1343, June 1960. (1140 N. E. 163rd St., North Miami Beach, Fla.)

Stress thrombosis of the subclavian and/or axillary veins may occur from indirect trauma, the two factors operating to produce the thrombosis being vessel damage, including stretching, and slowing of the blood flow. Clinically, the disease occurs predominantly in males, with the highest peak of incidence in the third decade. A history of heavy work or unaccustomed movement of the arm can usually be elicited. The most common symptoms are swelling, pain, and cyanosis, in that order, and examination reveals prominence of the superficial veins of the arm, shoulder, and upper thoracic wall.

The author reports the case of a 29-year-old stevedore, who experienced swelling of the left upper arm after some particularly hard work that involved heavy lifting, with subsequent pain and stiffness in the arm. Venography was performed about four months after the onset of symptoms and again after a two-year interval, when the patient was relatively asymptomatic. In the first venogram the axillary vein is clearly seen to narrow and finally disappear as it passes between the clavicle and the first rib. The second study revealed a marked increase in the collateral circulation of the entire shoulder girdle, but the narrowing and obliteration of the axillary vein between the clavicle and the first rib remain the same as they were two years previously. This finding reaffirms what has often been stated in the literature, namely, that, while arterial thromboses frequently recanalize, venous thromboses seldom do.

Many therapeutic procedures have been advocated, including thrombectomy, but the end-results have generally been disappointing regardless of the method employed. It is suggested that, since recanalization of the veins is unlikely and the threat of pulmonary embolism exists, ligation of the vein proximal to the thrombosis is a rational form of therapy.

Two roentgenograms.

CHARLES M. GREENWALD, M.D.
St. Cloud, Minn.

Percutaneous Splenoportal Venography, with Additional Comments on Transhepatic Venography. Sherwin S. Zeid, Benjamin Felson, and Leon Schiff. *Ann. Int. Med.* 52: 782-805, April 1960. (S. S. Z., VA Hospital, Long Beach 4, Calif.)

Between November 1956 and May 1958, percutaneous splenoportal venography was performed at the Cincinnati General Hospital (Cincinnati, Ohio) in 41 patients, ranging in age from three to seventy-seven years. In 8 patients the first attempt proved unsuccessful and the procedure had to be repeated, bringing the total number of examinations to 50. In 1 patient the intrasplenic pressure was measured but contrast medium was not injected.

All patients are hospitalized for the examination and appropriate preparatory measures and sensitivity tests are carried out. An intercostal approach has been employed except when the spleen is very large, in which event a subcostal route is used. With the patient in the supine position, a 3- or 3 1/2-inch 18-gauge needle, specially designed with four distal lateral holes, is inserted through the left ninth or tenth intercostal space in the midaxillary line, with stylet in place. The needle is directed medially and somewhat dorsocranially from the puncture site for a distance of 2 1/2 to 3 inches while the patient holds his breath in mid- or full inspiration. Best results have been achieved with the tip of the needle near the splenic hilus, well away from its point of entry into the spleen. Movement of the needle with respiration and a steady drip of blood through its lumen on removal of the stylet confirm its intrasplenic position. It is important that the needle move freely with respiration, since its fixation in a rib has been responsible for laceration of the spleen. A 10-inch long piece of flexible plastic tubing (with Luer-Lok connections), filled with saline, is locked to the needle hub and connected by a three-way stopcock to a saline-filled syringe. Intrasplenic pressure is then recorded, using a fluid manometer. The manometer is removed and the saline syringe is replaced by one containing the contrast material, usually 70 per cent sodium acetrizoate. During respiratory arrest, 25 to 35 c.c. of the medium is injected in four to six seconds and the needle is withdrawn. The first roentgenogram is exposed when half of the contrast material has left the syringe. Films are exposed at the rate of one a second for five seconds, then one every two seconds for six seconds, for a total of eight exposures. Recently a fifteen-second exposure has been added, and even later exposures are recommended. A fifteen-minute pyelogram should also be obtained.

In most of the patients in the present series, splenoportography was performed in an effort to differentiate between intrahepatic and extrahepatic block, and thereby to help determine the type of shunting operation indicated. It was also performed in selected cases with prior surgical portacaval anastomosis to determine the patency of the shunt, and in patients suspected of having esophageal varices.

Contraindications to the performance of percutaneous splenoportal venography include (1) inability of the patient to tolerate splenectomy; (2) sensitivity to the drugs to be employed; (3) renal insufficiency; (4) local disease along the needle pathway, such as left pleurisy with effusion; (5) bleeding tendency; (6) hemoglobin of less than 10 gm. per cent, and (7) splenic sepsis or conditions which predispose to rupture of the spleen.

No instance of splenic rupture or significant hemor-

rhage was encountered in the present series. In 2 patients a transient fall in systolic blood pressure of about 20 mm. was recorded shortly following splenoportography, but the hemoglobin and hematocrit values remained unchanged. Laparotomy was performed in 20 patients several weeks or less after the contrast study; in only 2 was an intraperitoneal hematoma found, in amounts of about 20 and 75 c.c., respectively. Abdominal pain of varying severity and duration following the procedure was experienced by a number of patients, but in only 15 were analgesics required for relief.

In 27 patients with cirrhosis there appeared to be no close correlation between the roentgenologic extent of the collateral circulation and such factors as the clinical signs, liver function tests, or even intrasplenic pressure. In this cirrhotic group, however, the pressures were significantly greater in those with a history of hematemesis than in those without. Percutaneous splenoportal venography proved to be more reliable in the diagnosis of varices than did the barium swallow. In 11 cases, barium swallow failed to reveal the gastric or esophageal varices demonstrated subsequently on the splenoportogram. It was found that failure of the contrast medium to enter the portal venous ramifications in the liver, or even to fill the extrahepatic portion of the portal vein, does not necessarily indicate extrahepatic block. Apparently the resistance in the liver may reverse the flow in the portal or splenic veins, so that contrast-laden blood bypasses the liver *via* the coronary and mesenteric veins and other collaterals. Even when an occlusion of the portal vein is found, it is not always at the site demonstrated by splenoportography. In patients in whom the roentgen findings suggest extrahepatic block, it is advisable at the time of operation to obtain a portal venogram or to take pressure readings on both the splenic and hepatic sides of the presumed occlusion.

The accidental injection of the liver during an attempted percutaneous splenic puncture led the authors to perform transhepatic venography in 3 patients. This procedure and its applications are discussed.

Nineteen roentgenograms; 2 tables.

GORDON L. BARTEK, M.D.
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Identification of Pelvic Masses by Phlebolith Displacement. Howard L. Steinbach. *Am. J. Roentgenol.* 83: 1063-1066, June 1960. (University of California Medical Center, San Francisco 22, Calif.)

Phleboliths are calcified thrombi which are attached to the wall of a vein by a thin pedicle or "tail." They are present in about one-third or one-fourth of all adult pelvises, the number increasing with age. Thus, phleboliths are most frequently present in older patients in whom pelvic masses are most likely to develop. The number of phleboliths in a pelvis may vary from 1 to 24, or more, but in four-fifths of all cases is less than 4. They are slightly more numerous in females than males. They are seen in the rectal and vesical venous plexuses of both sexes and in the broad ligament of the female and the prostatic venous plexus of the male.

The author has observed several patients in whom pelvic masses produced displacement of phleboliths. In most cases the mass was identified on plain roentgenograms, but in some instances the displaced phleboliths were the only roentgenologic manifestation. Two patients had abdominal perineal resections, and enema studies to demonstrate the pelvic viscera could not be

performed. In other patients, the response to roentgen therapy or surgical removal of a mass could be judged by a migration of the phleboliths toward their normal anatomic position. As expected, midline masses displaced the phleboliths laterally and produced an increased distance between the phleboliths on both sides of the pelvis. Lateral pelvic masses displaced the phleboliths medially. The phleboliths were also displaced superiorly or inferiorly depending upon the position of the mass. The phleboliths initially affected were those nearest the expanding lesion.

Ten roentgenograms. NORMAN L. ARNETT, M.D.
Anaheim, Calif.

THE DIGESTIVE SYSTEM

The Use of Contrast Medium in the Investigation of the Acute Abdomen. Eric Samuel. *Proc. Roy. Soc. Med.* 53: 393-398, June 1960. (Royal Infirmary, Edinburgh, Scotland)

The development of the triiodo compounds has made possible a water-soluble contrast medium which is fluid and yet possesses sufficient contrast for use in the diagnosis of acute gastrointestinal lesions. The author has employed Urografin 76 per cent combined with a nonionic wetting agent primarily for the investigation of hemorrhages from the upper gastrointestinal tract, leaks and perforations from the alimentary tract, and in the identification of the nature and site of intestinal obstruction. Contrast media have also been used for intravenous cholangiography and intravenous urography.

Hematemesis and Melena: With a water-soluble medium and meticulous attention to a "no-touch" technic, it has been possible to carry out roentgen examination of patients with hematemesis and melena immediately upon their admission to the hospital. The use of the supine position, while avoiding palpation of the abdomen, has been sufficient to outline the mucosal pattern of the stomach and duodenum. The density of the medium is surprisingly good. Its miscibility with intestinal contents is such that cavities and ulcers fill more readily than with barium sulfate. The presence of blood in the stomach, with clot formation, has not offered any difficulties in diagnosis. Usually the outline of the blood clot is smooth and well defined, distinguishing it from a new growth.

Perforations and Leaks: In 20 cases of suspected perforation, 14 positive diagnoses were made. Where a leak was detected, the course of the medium indicated the path of infection and the fistulous communication through the perforation was readily demonstrated. The investigation of cases of duodenal perforation has been limited to those in which the clinical diagnosis was indefinite or in which the plain films did not show evidence of pneumoperitoneum. Leaks from anastomotic lines are relatively easy to demonstrate. The outlining of the fistulous tracts has proved of considerable assistance in treatment.

Intestinal Obstruction: When the classical picture of intestinal obstruction is not present, the administration of an oral contrast medium may reveal the nature and the anatomical site of the affected loop. An oral medium has also been used to determine whether a true mechanical obstruction or an ileus exists. In vascular

occlusions, there may be only a localized area of paralytic ileus; in such cases the medium can be seen to pass through the affected area quite slowly, with the risk that a mistaken diagnosis of ileus may be made without due regard for the seriousness of the vascular obstruction.

Pancreatic Lesions: An oral contrast medium may assist considerably in the diagnosis of acute pancreatitis. Segmental pancreatitis involving the tail or body of the pancreas may be demonstrated by changes in the duodenojejunal flexure and the retrogastric portion of the stomach.

Cholecystitis: Unfortunately, plain roentgenograms of the abdomen are not often helpful in demonstrating calculi, being positive in only 25 per cent of a series of 200 cases of "acute abdomen" seen at the Royal Infirmary (Edinburgh). An intravenous contrast medium has been used to differentiate between acute obstructive and nonobstructive cholecystitis. With Biligradin, the patency (or otherwise) of a cystic duct can be recognized within two hours of the injection. Although it is theoretically possible for an acutely inflamed gallbladder to fill with Biligradin, this seldom occurs. Failure of visualization of either the extrahepatic ducts or the gallbladder following the injection of 20 c.c. of Biligradin Forte indicates that the liver has failed to concentrate the medium sufficiently, and no opinion on the state of the gallbladder can be expressed. If the extrahepatic ducts fill out normally but the gallbladder fails to fill in two hours, an obstruction of the cystic duct is usually present, but under certain conditions the gallbladder may fill at a later stage. A film at four hours may thus be desirable.

Urinary Tract: Intravenous urography may indicate the cause of an "acute abdomen." In a series of 200 consecutive cases of "acute abdomen," 16 were potentially renal lesions and, in these, calculi were seen on the plain film in only 2. Features found of value in the intravenous pyelogram are the prolonged nephrogram on the affected side, delay in appearance of the pyelogram, and distention of the renal pelvis and ureter as far as the site of obstruction if the case is followed for a sufficient interval.

[A word of caution: The aqueous contrast material may pass through an obstructing lesion of very small lumen and its saline cathartic effect may be detrimental to a dehydrated patient.—J. P. F.]

Seven roentgenograms; 3 diagrams.

JOHN P. FOTOPoulos, M.D.
Northwestern University Medical School

Radiology in Surgery of the "Acute Abdomen." H. Dendy Moore. *Proc. Roy. Soc. Med.* 53: 391-393, June 1960. (Exeter, Devonshire, England)

The author discusses the role of radiology in the differential diagnosis of the "acute abdomen," using the following headings: (1) in avoiding surgery for medical conditions, (2) to confirm or establish a diagnosis, (3) to decide on the correct treatment, (4) in the treatment of the "acute abdomen," (5) the unexpected.

(1) Patients with abdominal pain may actually have medical conditions, such as pneumonia or spinal disease. Abdominal pain in a 19-month-old boy, for example, could not be explained until roentgenograms showed the regular density of the diaphragms of the long bones produced by the deposition of lead phosphate which occurs in lead poisoning in children.

(2) When a diagnosis is in doubt, roentgenography may clarify the position. Examples given include trauma, perforated peptic ulcer, inflammation, and obstruction.

(3) It is better to begin an operation knowing the exact location of the lesion. In intestinal obstruction, the site of the block can often be demonstrated by a plain roentgenogram. In infants with imperforate anus, the operation performed when the gut is close to the anal dimple differs vastly from that necessary when there is wide separation. The site of perforation of a peptic ulcer may be shown by aqueous contrast materials.

(4) Intussusception can often be reduced completely and permanently by means of enemata under radiological control, while even partial reduction can simplify operation. In patients with volvulus of the sigmoid colon, emergency surgery can frequently be avoided by passage of a tube, through a sigmoidoscope, beyond the twist, thereby relieving the obstruction and allowing the bowel to be prepared for a one-stage operation.

(5) Roentgenograms may reveal a foreign body or other unexpected condition.

The author concludes that, although radiology in the "acute abdomen" may be misleading and in some instances may not be of help, it is much more often of value and often indispensable.

Five roentgenograms.

JOHN P. FOTOPoulos, M.D.
Northwestern University Medical School

The Use of Cinefluorography in the Routine Diagnosis of Disease of the Upper Gastrointestinal Tract. Experience in 1,000 Cases. Joseph Jorgens, Ilmar O. Kiesel, and Harlan W. Hawkinson. *Am. J. Roentgenol.* 83: 942-946, May 1960. (VA Hospital, Minneapolis 17, Minn.)

Using a standard fluoroscopic unit, an image amplifier, and a 16-mm. motion picture camera, the authors have performed over 1,000 examinations of the upper gastrointestinal tract in the past two years. The cinefluorograms were made during routine fluoroscopy. They have been substituted for most spot-films, though conventional post-fluoroscopic roentgenograms of the stomach and duodenum are still taken, as these portray better the relative size and position of the organs. Kodak Linagraph Shellburst film was exposed at either 15 or 30 frames per second and processed in standard solutions in the X-Ray Department. The film strips are viewed by projecting them on a white illu-trator type cardboard. When the entire upper gastrointestinal tract was cinefluorographed, the total air dosage was less than 120 r, with no one area receiving more than 50 r in air.

Cinefluorography was found to be most valuable in study of deglutition, the distal esophagus, the gastric antrum, and the duodenal bulb. The chief advantages of the procedures are: (1) the image amplifier provides a bright and detailed fluoroscopic image, (2) the camera records the characteristics of the peristaltic wave which may be of prime importance in the early detection of disease of the gastrointestinal tract, and (3) the motion picture film provides a permanent record of the fluoroscopic examination for study and reference. The main disadvantages of the cinefluorograph are: (1) it is somewhat heavy and awkward to handle, (2) the field

size is small, and (3) it is expensive to buy and maintain.

One photograph. RICHARD F. McCLURE, M.D.
Redondo Beach, Calif.

Experiences with Oral and Rectal Contrast Media in Pediatric Radiology. Armand E. Brodeur. *Missouri Med.* 57: 710-712, June 1960. (Cardinal Glennon Memorial Hospital for Children, St. Louis, Mo.)

The pediatric radiologist is frequently called upon to evaluate the suspiciously distended abdomen of a newborn infant. For this purpose, the author recommends Oral Hypaque, a contrast medium which is completely water-soluble, with "all the aqueous advantages of barium suspension without the attendant threats." Its density is satisfactory and can be immediately and effectively changed by the simple addition of more solution or powder for greater contrast and more water for lesser contrast if needed, as in the study of polyps. These advantages also hold in the examination of older children. In infants the nasogastric tube is a simple, safe, and effective method of filling the stomach. In the examination of older children, the bitter taste may be masked with Coca-Cola. Techniques are given for the use of the solution in colon studies, in fistulous tract injections, in the study of esophageal areas, and in small-bowel examinations.

A New Method for Roentgen Examination of the Fornix and the Cardial Region of the Stomach (Double Contrast Examination with Spray). M. Föti. *Radiol. clin.* 29: 101-108, March 1960. (In German) Röntgenabteilung des Hauptstädtischen Krankenhauses Budapest, Hungary.

The author uses a spray device connected to a gastric lavage tube with an olive tip for introduction of colloidal barium into the region of the gastric cardia and fornix. The olive tip should have holes along the side as well as at its end to get a diffuse spray into the area to be examined. A valve permits either inflation of the stomach with air or spray injection of the barium.

The stomach is aspirated and 200 to 300 ml. of air are injected into it (occasionally up to 1,200 ml.). A small amount of barium is then sprayed into the area to be studied.

Nine roentgenograms demonstrate the findings in normal cases, neoplasm, and high gastric ulcer.

JULIUS HEYDEMANN, M.D.
Chicago, Ill.

Effect of Gastric Intubation on the Normal Mechanisms Preventing Gastroesophageal Reflux. Richard Nagler, Alfred W. Wolfson, Robert M. Lowman, and Howard M. Spiro. *New England J. Med.* 262: 1325-1326, June 30, 1960. (Yale University School of Medicine, New Haven, Conn.)

Since prolonged intubation of the stomach has been implicated as a cause of peptic esophagitis, an attempt was made to determine whether gastric intubation with a Levin tube would lead to gastroesophageal reflux. The cardioesophageal function was studied radiologically in 20 patients, first before introduction of a Levin tube, ten minutes after the tube had been passed into the stomach, and again ten minutes after removal of the tube. The gastric contents were kept relatively con-

stant during the three examinations by giving the patient a sufficient quantity of barium to fill the stomach just before each test.

Gastroesophageal reflux was not demonstrated in any patient when the Levin tube was in place or after its removal. The gastric tube did not grossly affect the mechanical barriers to reflux in this short-term study. To answer the question whether more prolonged intubation would interfere with cardioesophageal function or cause reflux would require additional studies.

MORTIMER R. CAMIEL, M.D.
Brooklyn, N. Y.

Malignant Disease and Gastric Polyps. Leonard Breslaw. *California Med.* 92: 430-433, June 1960. (9735 Wilshire Blvd., Beverly Hills, Calif.)

A case report is used as the basis of a discussion of the relationship of gastric carcinoma to gastric polyps. The patient was a 65-year-old man with epigastric distress, bloating, and occasional cramp-like pain. X-ray examination revealed a polypoid lesion involving the anterior wall of the body of the stomach, midway between the greater and lesser curvatures. Because of slight irregularity and thickening of rugal folds adjacent to the lesion, the radiologist suggested the possibility of a cancer or lymphoma. Gastroscopecally, the polyp was identified and appeared benign by all the usual criteria; several smaller polyps were also seen. Six months later the x-ray picture was characteristic of cancer, although there had been no change in the symptoms. On exploration, metastasis to nodes, regional in nature, was already present. Histologic sections showed extensive antral gastritis and adenocarcinoma, with metastasis to regional lymph nodes.

The author re-emphasizes the importance of the study of mucosal detail in the area surrounding a gastric polyp. Other discussions of the incidence and malignant degeneration of benign lesions of the stomach are cited (Rigler and Erickson: *Radiology* 26: 6, 1936).

Fifteen roentgenograms; 1 photograph.

SYDNEY F. THOMAS, M.D.
Palo Alto, Calif.

Gastric Stump Carcinoma. D. Vajda, E. Nagy, and G. Molnár. *Fortschr. a. d. Geb. d. Röntgenstrahlen* 92: 653-658, June 1960. (In German) (Röntgenabteilung der III. Chirurgischen Klinik, Mező Imre ut 17, Budapest, Hungary)

Ten cases of primary carcinoma of the gastric stump are reported, and 2 cases of recurrent stump carcinoma are compared to them.

In the 10 cases of primary carcinoma, gastric resection had been performed two to thirty-one years previously for benign gastric or duodenal ulcer. Careful histologic examination of the specimens had revealed no sign of malignancy. Symptoms and signs associated with the carcinoma were pain, melena, hematemesis, weight loss, fetid eructations, an elevated erythrocyte sedimentation rate, but rarely a palpable tumor. Dysphagia was present if the lower esophagus was involved.

Primary carcinoma usually occurs in the proximal portion of the gastric remnant without involvement of the anastomosis. Most of the stump is involved. The air bubble shows a filling defect or is displaced. Obstruction may be present at the distal end of the esophagus. Differential diagnosis involves polypoid

"anastomosis" and recurrent stump carcinoma. In the former, involvement is localized, with smooth margins and normal adjoining mucosa. In the latter, the gastric remnant is hemispherically dilated and filled with secretions, due to anastomosal obstruction. Affluent loop obstruction may be present. Filling defects are evident at the anastomosis or in the adjoining stomach and small bowel.

Seven roentgenograms; 1 table.

EUGENE A. CORNELIUS, M.D.
Houston, Texas

Relationship Between Ulcers in the Aged and Radiologically Demonstrated Calcification of the Left Gastric Artery. J. Holstein and A. Stecken. *Fortschr. a. d. Geb. d. Röntgenstrahlen* 92: 644-652, June 1960. (In German) (Röntgenabteilung der I. Medizinischen Universitätsklinik und Poliklinik der Charité, Berlin, Germany)

Five cases of the simultaneous occurrence, in aged patients, of gastric ulcer and radiologically demonstrable calcification of the left gastric artery are reported. These cases were detected within a single year. In all there was also calcification of the abdominal aorta and, in some, of the coeliac artery and its branches. The calcification of the left gastric artery was demonstrated close to the lesser curvature and maintained a constant spatial relationship to the nearby ulcer in various positions. Kymographic pulsations characteristic of arteriosclerosis were frequently observed in the great vessels adjoining the heart.

The ulcers in these cases differed from the typical gastric ulcer, in that pain was minimal (2 cases) or absent altogether (3 cases). With medical management, healing was slow and there was a marked tendency to early recurrence.

The authors feel justified in using the clinical concept "ulcer of the aged" for these cases. They believe that a definite relationship exists between calcification of the left gastric artery and the occurrence of ulcer, since up to this time, every patient seen by them with radiologically demonstrable calcification had been found to have a gastric ulcer.

The possibility of this type of ulcer should be kept in mind in all patients over fifty years of age with mild upper abdominal symptoms and in patients with calcifications in the upper abdomen. Calcification in the renal or splenic arteries or in veins must be excluded.

Nine roentgenograms; 1 diagram.

EUGENE A. CORNELIUS, M.D.
Houston, Texas

Perforated Peptic Ulcer. Radiological Review of 50 Consecutive Cases. Charles Stuart. *J. Coll. Radiologists Australasia* 4: 32-38, June 1960. (Fremantle Hospital, Fremantle, Western Australia)

The radiologic findings in 50 consecutive cases of proved perforated peptic ulcer have been reviewed. Thirty-one of the ulcers were duodenal and 19 were gastric. Forty-two of the patients were males and 8 were females (a 5:1 ratio). The radiographic techniques employed in this series are those in general use. Free gas was identified in the peritoneal cavity in 44 patients (88 per cent); in 8, the gas was faintly visible, in 25 easily visible, and in 11 it was abundant. There did not appear to be any direct relationship between the time of perforation and the amount of free gas present,

nor between the amount of gas present and the size of the perforation. At operation, free fluid was found in the peritoneal cavity in all 50 cases. In most of these patients, roentgen examination had indicated the presence of varying amounts of fluid, and this is considered to be the second important point in the diagnosis of perforation. The free fluid and gastric contents produce a peritonitis, with the appearance of an adynamic ileus on the plain films. There are gas-fluid levels in both large and small bowel, and the bowel rises on the intra-abdominal fluid.

Pneumoperitoneum has been seen in perforation of the colon in ulcerative colitis, but this is uncommon. Rupture of the jejunum and small bowel rarely produces free gas in the peritoneal cavity. Consequently, the presence of free gas in the peritoneum almost always signifies perforation of the stomach or duodenum. Eight roentgenograms; 2 tables.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

The Roentgenologic Diagnosis of Gastrocolic and Gastrojejunalic Fistulas. Robert H. Thoeny, John R. Hodgson, and Harold H. Scudamore. *Am. J. Roentgenol.* **83**: 876-881, May 1960. (The Mayo Clinic, Rochester, Minn.)

Gastrojejunalic fistulas constitute a serious sequela of the surgical treatment of peptic ulcer and cancer. The great majority of these fistulas result from perforation of a jejunal or gastrojejunal ulcer at or near the site of a gastroenterostomy opening. They occur almost exclusively in men. The average time between the original surgical treatment and the formation of the fistula is about five years.

Gastrocolic fistulas result primarily from perforation through carcinomas of the stomach or colon—usually the larger, more advanced neoplasms. Here no marked sex predilection is apparent. In a patient who has had a gastroenterostomy or who has a malignant abdominal tumor, the classic symptoms of diarrhea, weight loss, and fecal eructation or vomiting strongly suggest the presence of a fistula between the stomach and the colon. Roentgenologic techniques provide the most accurate means for diagnosis. A barium-enema examination will demonstrate the fistula in almost 100 per cent of cases; a barium meal frequently fails to do so. During the barium-enema study, the roentgenologist notes filling of the stomach and jejunum with barium from some point in the left transverse colon. Often the exact site of the fistula is difficult to determine, and usually it is impossible to distinguish between the two types.

The roentgen findings in 60 gastrojejunalic and gastrocolic fistulas, in 59 patients, seen at the Mayo Clinic between 1947 and 1958 are presented. In 18 patients the fistula was associated with carcinoma. In 12 of these cases a diagnosis of gastrocolic or gastrojejunalic fistula was made roentgenologically. Four of the 6 in whom no fistula was demonstrated were given barium by mouth only. A correct diagnosis was made in 11 of 13 patients examined by barium enema and in only 3 of 9 examined with a barium meal.

Forty-one of the fistulas had been formed by perforation of a jejunal or gastrojejunal ulcer in patients previously operated on for duodenal ulcer (gastroenterostomy in 31 instances and partial gastrectomy in 10). One fistula occurred in a patient with chronic

ulcerative colitis. A correct diagnosis was made roentgenologically in 38 of the 42 cases. Barium-enema examination was performed in 30 patients with demonstration of the fistula in every instance. Among 35 examinations with barium by mouth, fistula was reported initially in only 4.

During the period in which the above 59 patients were seen, 7 additional patients were observed in whom a diagnosis of fistula was made when none existed.

Four roentgenograms; 2 tables.

RICHARD F. MCCLURE, M.D.
Redondo Beach, Calif.

The Big Duodenum. Harry W. Fischer. *Am. J. Roentgenol.* **83**: 861-875, May 1960. (University Hospitals, Iowa City, Iowa)

When interference with emptying of a hollow viscus occurs, the organ dilates. So it is with the duodenum. Not all obstructions of the duodenum are mechanical in nature, nor do all dilatations of the duodenum signify the presence of mechanical obstruction. In this paper the author discusses several aspects of dilatation of the duodenum without discontinuity of the lumen. Duodenal enlargement of this nature can be of two types. First, the duodenum may dilate secondary to a lesion distal to it; secondly, dilatation may result from interference with the contractility of the bulb and loop themselves, with the lower intestines being essentially normal.

Meschan *et al.* (*South. M. J.* **46**: 878, 1953. *Abst. in Radiology* **63**: 134, 1954) found that the diameter of the second portion of the duodenum is almost invariably 2 cm. The width of the rugae is also very constant, being 0.3 cm. in mid-duodenum. In their series, the duodenal bulb never exceeded 3.5 cm. at its base with a usual measurement of 3 cm.; it was never more than 4 cm. in height from pylorus to apex and usually measured 3 cm. Any increase over these values should suggest a megaduodenum.

A true megaduodenum must be seen repeatedly on multiple roentgenograms and at fluoroscopy. The roentgen criteria for the diagnosis should also include the observation of prolonged retention of barium. Another observation is a cascade effect of the barium dripping from the bulb into the dilated loop when the patient is in the erect position. In duodenal dilatation of the type under discussion, there must be an absence of encroachment upon the lumen by a lesion of any kind.

The author classifies megaduodenum with continuity of the intestinal lumen as follows: (1) Dependent upon influences mediated through the intact central and autonomic nervous systems (paralytic ileus of the duodenum): (a) pancreatitis; (b) cholecystitis, enteritis, and other inflammatory entities; (c) peptic ulcer; (d) emotional states; (e) trauma. (2) Dependent upon lesions in the extrinsic nervous system: (a) surgical—postvagotomy; (b) neuropathic—diabetes, vitamin deficiency, porphyria, inflammation. (3) Dependent upon abnormality of nerve and muscle of bowel wall: (a) congenital aganglionosis; (b) degenerative or toxic ganglion cell disease—scleroderma, porphyria, vitamin deficiency, electrolyte imbalance; (c) local vascular disease—lupus, purpura; (d) abdominal adhesions; (e) local muscle disease—dermatomyositis, hypoproteinemia.

The author states that it is not his intent to minimize

the significance of the large duodenum secondary to organic occlusion of the distal lumen, but to point out the importance of motor dysfunction of the duodenum and upper jejunum. It is necessary to realize that the lumen of the intestine may remain open and yet intestinal contents may not pass through efficiently. Minimal roentgen changes are reluctantly accepted as of clinical importance. When the findings become extreme, it is much easier to attribute symptoms to the physiologic and anatomic abnormality.

Eight illustrative cases are reported.

Nine roentgenograms.

RICHARD F. McCLURE, M.D.
Redondo Beach, Calif.

Malabsorption Syndromes: A Symposium. Brit. J. Radiol. **33**: 201-242, April 1960.

At the Annual Congress of the British Institute of Radiology in December 1959, a symposium on malabsorption syndromes was held, comprising five papers. Abstracts of these contributions follow.

I. Classification of Malabsorption Syndrome. C. C. Booth. Brit. J. Radiol. **33**: 201-211, April 1960. (Postgraduate Medical School of London, England)

Malabsorption syndromes are usually caused by defective digestion or absorption in the small intestine but may also be associated with abnormalities of the stomach. In many patients there is malabsorption of fat, causing steatorrhea and diarrhea, but malabsorption may involve other substances without affecting fat absorption. For this reason the term "malabsorption syndrome" rather than steatorrhea is generally used to describe the whole group of conditions.

The author suggests the following classification although it is not complete since there are some patients who will not fit into the described categories.

- A. Due to Defects of Gastric Function
 1. Postgastrectomy steatorrhea
 2. Deficient secretion of the intrinsic factor (addisonian pernicious anemia, total or partial gastrectomy)
- B. Due to Defects of Digestion
 1. Deficiency of bile (biliary obstruction)
 2. Deficiency of pancreatic enzymes (cystic fibrosis of pancreas, pancreatitis, pancreatectomy)
- C. Due to Defects of Intestinal Absorption
 1. Anatomical lesions of the small intestine
 - (a) Resection (proximal or distal)
 - (b) Bacterial contamination of small intestine (blind loops, strictures, fistulae, diverticulosis)
 - (c) Mixed lesions (resection plus loops, strictures, or fistulae)
 2. Lesions of the intestinal mucosa
 - (a) Localized (jejunitis or ileitis)
 - (b) Generalized (celiac disease, idiopathic steatorrhea, tropical sprue, infiltrations)
 3. Vascular lesions (mesenteric vascular occlusion)
 4. Drugs (certain antibiotics)
 5. Parasitic infestation (*Dibothriocephalus latus*, giardiasis)

Nine figures, including 2 roentgenograms.

D. KEITH EARDLEY, M.D.
University of Florida, Gainesville, Fla.

II. Radiological Investigation of Malabsorption Syndromes. J. W. Laws and R. G. Pitman. Brit. J. Radiol. **33**: 211-222, April 1960. (Radiodiagnostic Department, Hammersmith Hospital and Postgraduate Medical School of London, England)

The authors divide the malabsorption syndromes into two groups according to the main radiological features.

Group I: Radiological Features Predominantly Associated with Steatorrhea

- A. Generalized lesions of the intestinal mucosa
 - Celiac disease
 - Idiopathic steatorrhea
 - Tropical sprue
 - Infiltrations: Whipple's disease, scleroderma, amyloidosis, Hodgkin's disease, lymphosarcoma
- B. Defects of digestion
 - (a) Deficiency of bile: obstructive jaundice, biliary cirrhosis
 - (b) Deficiency of pancreatic enzymes: cystic fibrosis, chronic pancreatitis, pancreatectomy
- C. Postgastrectomy steatorrhea

Group II: Conditions with Specific Radiological Features

- A. Localized lesions of the intestinal mucosa
 - Jejunitis
 - Regional ileitis
- B. Anatomical lesions of the small intestine
 - (a) Resection: proximal, distal
 - (b) Bacterial contamination: diverticulosis, blind or stagnant loop, stricture, fistula
 - (c) Mixed lesions (resection plus bacterial contamination)

In Group I the radiological changes are predominantly those associated with steatorrhea, namely, flocculation of the barium suspension and dilatation of the small bowel. In this group the changes are frequently non-specific, and radiology is of little value in differentiating between the underlying pathological lesions. In Group II the anatomical lesions are more demonstrable and specific, and it is in this group that radiology is of great value and is frequently the only method of arriving at a diagnosis.

Nineteen roentgenograms.

D. KEITH EARDLEY, M.D.
University of Florida, Gainesville, Fla.

III. The Haematological Diagnosis of Addisonian Pernicious Anaemia and the Intestinal Malabsorption Syndrome. D. L. Mollin. Brit. J. Radiol. **33**: 222-228, April 1960. (Postgraduate Medical School of London, England)

Severe megaloblastic anemia in an otherwise normal person is almost invariably due to Addison's pernicious anemia or to intestinal malabsorption syndrome. If the anemia responds completely to small intramuscular injections of vitamin B₁₂, the patient has Addison's pernicious anemia or the megaloblastic anemia associated with gastrectomy or anatomical lesions of the small intestine. If the anemia fails to respond or responds incompletely to B₁₂, then the patient is usually suffering from idiopathic steatorrhea. In many cases, however, the hematological signs of B₁₂ and folic acid deficiency are much less obvious, and in such instances newer methods of diagnosing these deficiencies are of

value. Methods of determining vitamin B₁₂ and folic acid levels and absorption are discussed.

The hematological, microbiological, and radiobiological studies which may be used to help diagnose and differentiate Addison's pernicious anemia and intestinal disorders associated with deficiency of B₁₂ and folic acid are summarized in a table.

D. KEITH EARDLEY, M.D.
University of Florida, Gainesville, Fla.

IV. The Radiological Features of Pernicious Anaemia. J. W. Laws and R. G. Pitman. *Brit. J. Radiol.* **33**: 229-237, April 1960. (Radiodiagnostic Department, Hammersmith Hospital and Postgraduate Medical School of London, England)

Seventy-one patients with proved pernicious anemia were examined to determine the radiological features, and, particularly, to ascertain the frequency with which gastric atrophy could be recognized radiologically.

Four radiological features were associated with a diagnosis of gastric atrophy: a tubular shaped stomach, a small volume of retained barium, a so-called "bald" fundus (absence of mucosal folds), and thin, crenated mucosal folds resembling crumpled tissue paper. No single feature was characteristic. If three features were seen in any one patient the diagnosis was considered established.

A positive diagnosis of gastric atrophy was made by a combination of radiological features in 38 of the authors' 71 patients (54 per cent) with pernicious anemia. Gastric atrophy was also strongly suspected in 17 others. Five patients in the series had gastric carcinoma and 1 a gastric polyp. The frequency of these two complications is discussed.

Gastric atrophy may also precede the development of subacute combined degeneration of the cord. The authors suggest, therefore, that a radiological diagnosis of gastric atrophy should make physicians watchful for the early manifestations of that condition.

Sixteen roentgenograms; 3 tables.

D. KEITH EARDLEY, M.D.
University of Florida, Gainesville, Fla.

V. Histopathology of the Stomach in Pernicious Anaemia and Jejunum in Steatorrhea. I. Doniach and Margot Shiner. *Brit. J. Radiol.* **33**: 238-242, April 1960. (Postgraduate Medical School of London, England)

In a postmortem study pernicious anemia has been shown to result in diffuse atrophy of the mucosa of the fundus and body of the stomach (but not of the pyloric antrum) and atrophy of the muscle coats of the body. In some cases there is total loss of body chief and parietal mucosal glandular cells without inflammatory change: gastric atrophy. In others, there are occasional scattered surviving specialized cells and quite well marked interstitial infiltration with lymphocytes and plasma cells: atrophic gastritis. With the use of the flexible gastric biopsy tube, studies of the gastric mucosa can be made in the living. The findings thus obtained confirm the postmortem studies but reveal a much higher case incidence of survival of scattered parietal and body chief cells than had been formerly recognized.

The authors report biopsies of the upper jejunum in 41 cases of steatorrhea and 10 normal controls. They classify their findings into normal, subtotal villous

atrophy, and partial villous atrophy. On this basis and comparison with the observations of others, it is concluded that in established celiac disease and idiopathic steatorrhea there is well marked villous atrophy and glandular hypertrophy of the jejunal mucosa, and that any reversal to normal villous formation is excessively rare, in spite of clinical remission in response to a gluten-free diet. On the other hand, in tropical sprue and in those instances of villous atrophy which occur in a small proportion of cases of postgastrectomy steatorrhea due to small intestinal strictures or loops, reversal to normal mucosa as a result of treatment is likely to prove the rule rather than the exception.

Six photomicrographs; 1 table.

D. KEITH EARDLEY, M.D.
University of Florida, Gainesville, Fla.

Late Involvement of the Alimentary Tract by Carcinoma of the Kidney. Mansho T. Khilnani and Bernard S. Wolf. *Am. J. Digest. Dis.* **5**: 529-540, June 1960. (Mount Sinai Hospital, New York, N. Y.)

Six cases with involvement of portions of the digestive tract in carcinoma of the kidney—either as a result of metastasis or by direct extension—are reported. The gastrointestinal lesions became manifest from six months to fourteen years after removal of the original tumor. In 5 patients, involvement was the result of direct invasion by local recurrence. In these cases the roentgen findings were quite characteristic, consisting of a large polypoid or lobulated mass that occupied and distended the lumen. Obstruction, however, is not a prominent feature. Intussusception does not occur because of extrinsic fixation. It is likely that these findings are the result of the fact that hypernephroma produces little fibrous tissue reaction or scirrhous response, and growth continues as the mass protrudes into the lumen. Eventually, unless the patient dies from other manifestations of the neoplasm, ulceration of the mucosa over the tumor occurs and gastrointestinal bleeding results. When the site of the mass in the gastrointestinal tract is related to the kidney bed and, in addition, a soft-tissue density outside and adjacent to the involved segment of bowel is seen, there is no difficulty in arriving at a correct diagnosis.

In 1 of the authors' 6 cases, a metastasis to the upper jejunum was found two years after resection of the primary kidney carcinoma. This produced intermittent intestinal obstruction as a result of intussusception.

Nine roentgenograms. JOHN F. RIESSER, M.D.
Springfield, Ohio

Polycystic Disease of the Liver, with Unusual Cholecystographic Manifestations. Report of a Case. Earl E. Gambill and John R. Hodgson. *Gastroenterology* **38**: 1003-1004, June 1960. (The Mayo Clinic, Rochester, Minn.)

A case of polycystic disease of the liver, with unusual cholecystographic manifestations, is reported. In 1948, a diagnosis of polycystic disease was made in a 49-year-old woman. For the next eleven years roentgen examinations of the stomach and gallbladder were done several times yearly, often at the patient's insistence. Results of these examinations were normal until 1959, when most unusual cholecystograms were obtained. These are reproduced and show marked distortion and irregularity of the gallbladder shadow due to extrinsic pressure exerted by multiple cysts in the liver. The

authors know of no other condition that will produce this unique appearance.

MAJ. MARTIN A. THOMAS, M.C.
Lackland AFB, Texas

Diagnostic Radiology of the Cystic Duct. Lidio G. Mosca and Nélida V. Di Rienzo. *Radiologia* 10: 101-113, June 1960. (In Spanish)

This is a review of cystic duct radiology based upon previous reports in the literature, without specific reference to personal experiences.

The authors point out that a stump of cystic duct which has been left after cholecystectomy predisposes to and sometimes causes the post-cholecystectomy syndrome. Stone, amputation neuroma, or choledocholithiasis may occur and produce intermittent colic and/or jaundice. The diagnosis can be made by intravenous cholangiography. Administration of morphine sometimes improves visualization and identification of duct stumps.

Dilatation of the common duct occurs frequently in the presence of cystic duct stumps, and indicates choledocholithiasis.

Stones are usually missed radiographically, and may cause sclerosis or atrophy, so that the stump also is missed. For this reason radiographically negative examinations do not rule out a diagnosis.

Accumulation of medium in the duodenum in intravenous cholangiography sometimes produces a confusing shadow lateral to the common duct. This the authors have been able to dispel by giving the patient a glass of water.

Eleven roentgenograms; 5 diagrams.

DON E. MATTHIESEN, M.D.
Phoenix, Ariz.

Cholangiomanometric Interpretation of Lesions in the Main Biliary Duct: 800 Peroperative Examinations. A. A. Arianoff and E. H. Henrard. *J. belge de radiol.* 43: 227-237, 1960. (In French) (Brussels, Belgium)

The authors have developed a technic of "serial peroperative cholangiography under manometric control" and report its use in 800 cases. Introduction of a non-irritating medium at physiological pressure allows investigation not only of the anatomical outline of the biliary tree and of its normal dynamism, but also of its response to various pressures. By the use of antispasmodics and multiple films, it is possible to study the mechanism of action and dynamics of the biliary system as well as that of the pancreato-biliary junction.

The authors distinguish different lesions of the main biliary duct which are secondary to biliary affections. Some of these are functional and reversible, while others are organic and permanent. Their radiographic and manometric study furnishes information about either the necessity of immediate therapeutic measures or the abstention from dangerous and prejudicial surgery. Five stages of disease of the main biliary duct, following one another in chronological order, are described: terminal choledochitis, acute hemorrhagic pancreatitis, satellite pancreatitis, organic Odditis with low inferior pancreatitis, and chronic pancreatitis of the head. The radiologic aspect of the duct in each of the five stages, and of the duodenal passages, is described, and the residual intracholedochal pressures are recorded.

It may be concluded from this study that operative

cholangiography alone is not sufficient for exact and complete diagnosis of the lesions associated with biliary disease, and that manometric procedures are indispensable for correct interpretation.

PETER TORBEY, M.D.
University of Missouri

A Statistical Comparison of Orabilex and Telepaque. Richard M. Friedenberg, Victor Sayegh, and R. J. Schulz. *Am. J. Digest. Dis.* 5: 564-572, June 1960. (Lebanon Hospital, Bronx, N. Y.)

A total of 120 examinations on 87 patients were performed in a "blind study" of the effects of Orabilex (4.5 gm.) and Telepaque (3.0 gm.). Twenty patients receiving both media, with at least two weeks between tests, were cross-examined. Each patient was evaluated as to the degree of opacification of the gallbladder, the presence or absence of calculi, the degree of fatty-meal contraction, opacification of the biliary ducts, the amount of residual medium in the digestive tract, and the occurrence of side-reactions. The data obtained were analyzed by standard statistical methods; the results of this statistical comparison indicated no significant difference between the contrast media tested in any of the above categories.

The strong subjective element in such a study is stressed. In many cases, two observers noted their findings independently to allow comparison of the subjective responses.

Telepaque provided slightly better visualization of the gallbladder and common bile duct. Orabilex left less intestinal residue than Telepaque and produced fewer side effects. Telepaque caused diarrhea primarily, while Orabilex led to nausea. Both media were judged excellent for opacification of the gallbladder, with a minor degree of side reaction, but neither can be called ideal.

Seven tables.

JOHN F. RIESSER, M.D.
Springfield, Ohio

Intravenous Cholangiography and Tomography as an Aid in the Diagnosis of Ascariasis of the Biliary Tract. S. Cywes and H. Krige. *South African M. J.* 34: 478-479, June 4, 1960. (Groote Schuur Hospital, Cape Town, Union of South Africa)

Ascariasis of the biliary tract is not uncommon in Cape Town (South Africa), especially in children. Since Biligrafin became available in 1957, the authors have found intravenous cholangiography and tomography useful means of confirming the clinical diagnosis. These studies can be done as out-patient procedures. Once the diagnosis is made, conservative treatment has proved highly successful and the need for laparotomy has not arisen. An illustrative case is reported.

The authors were unable to find in the literature any reference to this confirmatory roentgen method in biliary ascariasis.

One roentgenogram.

Residual Contrast Medium in the Bowel in Cholecystography with Iopanoic Acid and Certain Related Substances. Lars Andrén and Georg Theander. *Acta radiol.* 53: 371-376, May 1960. (Malmö Allmänna Sjukhus, Malmö, Sweden)

Dense granules often observed in the bowel during cholecystography with iopanoic acid (Telepaque, Biliodon) may confuse the interpretation of the cholecystogram. The authors attempted to facilitate the ab-

sorption of iopanoic acid by using its sodium salt, Biliiodon-Natrium (Bi-Na). On exposure to the hydrochloric acid of the stomach, this is converted into an amorphous form of iopanoic acid having a larger surface area per unit of weight than the crystalline form (Telepaque and Biliiodon tablets). No significant decrease in the incidence of residues was noted with the new medium.

The sodium salt was then used with an enteric coating. Subsequently, attempts were made to neutralize the hydrochloric acid in the stomach by the administration of an antacid drug in association with the Bi-Na. Still no decrease in the incidence of residues resulted. These failures suggested that the residual granules did not consist mainly of iopanoic acid. Attention was therefore focused on iopanoic acid products of low solubility, namely, aluminum, calcium, iron, and magnesium salts. A chelating agent, EDTA, did not prevent the formation of the calcium salt of iopanoic acid from Bi-Na in water from the authors' district.

Twelve patients were then deprived of all foods, drugs, and beverages except distilled water, from the intake of the Bi-Na to the completion of the cholecystographic examination. In this series residues were found in 30 per cent, as compared to 80 to 90 per cent of patients examined by other methods. The authors conclude that the properties of water are important for the utilization of iopanoic acid in cholecystography. A similar role may be played by water in the absorption of drugs with a tendency to form salts of low solubility. Treatment with such drugs might be more or less effective in different regions depending on variations in hardness of the water supply.

Two tables. HAROLD A. SWANSON, M.D.
Calgary General Hospital, Calgary, Alta.

A Clinical Aid in Operative Cholangiography. John K. Stevenson and Lloyd M. Nyhus. Surg., Gynec. & Obst. 110: 759, June 1960. (University of Washington School of Medicine, Seattle, Wash.)

To decrease the technical problems inherent in operative cholangiography, the authors have modified two of the simple instruments employed in this procedure. After exposure and isolation of the cystic duct, a short-bevel 18- or 20-gauge needle is inserted into its lumen. This needle has been angled 30° from the axis of the shaft, approximately 1/2 to 3/4 inch from the tip. The needle is readily held in place by a specially devised holding clamp, modified from an ordinary blunt-tipped right-angle clamp. The serrations were removed from the ordinary clamp and a hole was bored between its jaw large enough to hold loosely the modified spinal needle. The modified clamp holds the needle snugly within the cystic duct during injection of the contrast medium and does not obscure the common duct during the x-ray exposures.

Two photographs. WALTER EATON, M.D.
University of Pennsylvania

HERNIA

X-Ray and Clinical Features of Hiatal Hernia. Significance of Hiatal Hernias of Minimal Degree. Henry J. Tumen, George N. Stein, and Elliott Shlansky. Gastroenterology 38: 873-883, June 1960. (1900 Rittenhouse Square, Philadelphia 3, Penna.)

The authors maintain that with a meticulous roentgenologic technic small hiatal hernias can be demon-

strated in a much greater percentage of patients than is generally reported. The procedure employed has been described by Stein and Finkelstein (Am. J. Digest. Dis. 5: 77, 1960. Abst. in Radiology 75: 988, 1960). The patient must be recumbent and in the right anterior oblique position for Bucky films exposed with the tube over the table, or in the left posterior oblique position for spot-filming with the fluoroscopic tube. The authors did not find that the Trendelenburg position added to their ability to demonstrate hiatal hernia.

The opinion is expressed that study of small sliding hiatal hernias will be facilitated if they are classified as follows: Grade I: herniation of only the gastroesophageal vestibule; Grade II: herniation of the gastroesophageal vestibule plus approximately 2 or 3 cm. of the cardiac end of the stomach; Grade III: herniation of 4 or 5 cm. or more of the cardiac end of the stomach.

Roentgenograms of 300 consecutive patients who had had upper gastrointestinal studies were reviewed; 169 of the patients were believed to have had adequate x-ray examination of the cardioesophageal area. Of these 169 patients, 72 had no symptoms suggestive of hernia, 24 had inconclusive symptoms, and 73 were considered to have characteristic hernia symptoms. Roentgen evidence of hiatal hernia was found in 113 of the 169 patients. Hernias were demonstrated in 38 of the 72 who were classified as clinically negative for hernia and in 62 of the 73 in whom a clinical diagnosis of hiatal hernia had been made. It is emphasized that, because of the selection of patients, this does not indicate the actual incidence of hernia in the general population.

Of the 113 hiatal hernias found, 86 (76 per cent) were classified as Grade I, 21 (18 per cent) as Grade II, and 6 (6 per cent) as Grade III. The mechanism of symptom production in Grade I hernias is not entirely clear. A constant relation between symptoms and regurgitation into the esophagus could not be demonstrated in these patients, but it may be an important factor. Regurgitation occurred in 18 of the 35 patients with Grade I hernias and typical symptoms of hernia and in only 2 of 12 patients who had hernias but no symptoms. A high incidence of heartburn in patients with Grade I hernias and hiatal symptoms suggests that disturbed motility of the lower esophagus may also be a basis for symptoms.

[Dr. F. E. Templeton, of Seattle, Wash., in his discussion of this paper (pp. 885-887) speculates that the so-called "Grade I hernias" may actually represent a normal anatomical feature. He does not differentiate between "vestibule" and "phrenic ampulla."—M. A. T.]

Sixteen roentgenograms; 5 tables.

MAJ. MARTIN A. THOMAS, M.C.
Lackland AFB, Texas

THE MUSCULOSKELETAL SYSTEM

On the Incidence of Senile Osteoporosis. Richmond W. Smith, Jr., William R. Eyler, and Raymond C. Mellinger. Ann. Int. Med. 52: 773-781, April 1960. (The Henry Ford Hospital, Detroit 2, Mich.)

The authors determined the incidence of senile osteoporosis in 218 ambulatory women, over forty-five years of age, seen as out-patients at the Henry Ford Hospital (Detroit, Mich.) for nondisabling disorders. Excluded were patients who had diseases which may result in osteoporosis, such as hyperthyroidism, rheumatoid arthritis, multiple myeloma, uncontrolled dia-

betes mellitus, or any illness requiring prolonged corticosteroid therapy. For the roentgen evaluation a single lateral view of the dorsolumbar spine centered at the thoracolumbar junction was employed. On the basis of the roentgen findings, patients were placed in one of five groups:

Normal: 124 patients (57 per cent)

Indeterminate: Borderline or equivocal findings. Questionable loss of bone density and trabecular thinning. No vertebral body deformity. 30 patients (14 per cent).

Grade 1: Overall density loss and trabecular thinning. End-plate accentuation and deformity. Early biconcavity and minimal vertebral wedging. 54 patients.

Grade 2: Further loss of density and of trabecular markings. End-plate deformities and biconcavities. Definite wedging of one or more vertebral bodies. 7 patients.

Grade 3: Severe demineralization. Extensive biconcavities. Marked wedging or collapse of several vertebral bodies. 3 patients.

As will be seen from the above classification, 64 women (29 per cent) had changes indicative of vertebral atrophy, yet only 10 of these had significant vertebral wedging. Only 23 per cent of the patients with osteoporosis were under fifty years of age; the majority were between sixty and sixty-five.

Back pain or distress was a major complaint for only 3 of the 124 women whose roentgenograms were normal although, when questioned, 24 others admitted having some form of back distress. Thus, 27 non-osteoporotic women (22 per cent) had symptoms possibly referable to the vertebral column. Nine of the 64 patients with roentgenologically demonstrable osteoporosis listed back pain as the chief complaint, while 13 others acknowledged such distress when specifically questioned—a total of 22 women, or 34 per cent. None of the 3 women with Grade 3 osteoporosis mentioned back distress in her medical history.

Other writers have estimated that more than a half of women over fifty years of age have x-ray evidence of decreased bone mass. The data of the present report do not appear to support this conclusion, since only 29 per cent of the 218 women were considered to have vertebral osteoporosis. In 30 women (14 per cent), however, the findings were indeterminate. That 1 woman in 5, aged fifty to fifty-four, has vertebral atrophy is perhaps the most significant finding of the present survey.

The role of gonadal involution and the loss of adrenal anabolic hormones in the pathogenesis of osteoporosis is discussed. When the results of the present survey are plotted graphically, a biphasic incidence curve is suggested. The first phase represents osteoporosis resulting from gonadal involution, with a peak incidence of sixty to sixty-four years, approximately ten to fourteen years after average physiologic menopause. In women not biologically destined for menopausal osteoporosis, bone atrophy does not develop until later years, when the more universal senile osteoporosis occurs following the decline of adrenal anabolic hormone secretion. This group is represented by the second phase of the incidence curve.

Similar studies of much larger patient and general population groups may yield information of pathogenetic significance, particularly when data of a clinical and biochemical nature are compared between osteoporotic

and non-osteoporotic contemporaries. Accumulating evidence that anabolic hormone therapy may arrest symptomatic osteoporosis makes clinically significant the detection of early vertebral atrophy in otherwise normal, asymptomatic women.

Two graphs; 2 tables. GORDON L. BARTER, M.D.
Grand Rapids, Mich.

Skeletal Changes in Burned Patients. V. Štěpánek and R. Doleček. Radiol. clin. 29: 82-94, March 1960. (In English) (Regional Hospital Ostrava V, Paskov, Czechoslovakia)

Since little is known about the skeletal changes in burned patients, the authors obtained roentgenograms of 40 persons with severe second- to fourth-degree burns affecting more than 40 per cent of the body surface. In most cases the roentgenograms were made two to four months following the injury. Four cases are reported in detail.

Osteoporosis was demonstrated in 8 cases and in 3 of these took the form of a typical Sudek's bone atrophy. An unburned area was the site of this change in 1 instance. Calcium deposits were found in the soft tissues of 3 patients.

The osteoporosis is attributed in part to neurovascular, neurotrophic changes, representing a local reaction to the damage sustained. There also develops a chain of complex reactions of both the nervous and endocrine systems. The reduced mobility, hypercorticalism, and other changes incident to this response (general adaptation syndrome of Selye), as well as hypoproteinemia, due probably to an increased production of glucocorticoids, also play a role.

The authors point further to disturbances in the "life of bones" and calcium metabolism in burned subjects. These disturbances are only sometimes demonstrable, but they must be assumed to a minor or major degree in all more serious burns.

Osteoporosis is not a change specific for burns; it represents only a part of nonspecific reactions elicited by a burn. In a rational treatment the influencing or blocking of these reactions must be considered because they can be often exaggerated and very harmful.

Five roentgenograms; 4 tables.

JULIUS HEYDEMANN, M.D.
Chicago, Ill.

The Rare "Os Supracoracoideum." G. Lisch. Radiol. clin. 29: 71-74, March 1960. (In German) (University of Pisa, Italy)

A small bone of conical shape about 1.0 cm. high is occasionally seen adjacent to or on the superior surface of the coracoid process; it may be fused with the coracoid or connected by a narrow joint. The regular bone structure and the presence of such a joint distinguish os supracoracoideum from post-traumatic calcification of the coracoclavicular ligaments, persistent epiphysis of the coracoid process, coracoclavicular bursitis, and avulsion of the upper surface of the coracoid process.

Two roentgenograms. JULIUS HEYDEMANN, M.D.
Chicago, Ill.

Adamantinoma of the Capitate Bone. W. P. Diepeveen, G. H. Hjort, and O. Ch. Pock-Steen. Acta radiol. 53: 377-384, May 1960. (The Finsen Institute, Copenhagen, Denmark)

The authors report a case of adamantinoma of the

capitate bone. Thirty-nine cases of adamantinoma affecting the long bones are said to have been recorded, but localization in the carpal bones had not been previously described. Roentgenologically, adamantinoma has a multicular, cyst-like appearance and, as it spreads gradually, the bone assumes a spindle shape. The tumor has a tendency to grow in the longitudinal direction of the bone, propagating exclusively in bony tissue. Periosteal reaction is seldom observed, although the cortex is eventually entirely destroyed. Secondary calcium deposits are not found in the tumor and spicules have not been reported. Although the degree of malignancy is low, metastases have been observed in several cases.

The authors' patient was a 72-year-old woman who had sustained an injury to the right wrist fourteen years previously. Two years later weakness of the hand developed, and four years before the examination, increased swelling. Roentgen examination disclosed complete destruction of the capitate bone as well as small cyst-like areas of destruction at the base of the third metacarpal and in the hamate bone. A subsequent examination, after three and a half months, revealed further destruction at the base of the third metacarpal bone and halisteresis of all the bones of the hand. The patient was not seen again for three years, at which time roentgenograms showed marked destruction of several carpal and metacarpal bones; the third metacarpus was completely destroyed. A biopsy of the tumor was performed, and the histologic diagnosis was glomangioma. Arteriographic findings, however, suggested a malignant lesion, and amputation of the forearm was performed. Histologically, the tumor was considered to be a synovial sarcoma, but an adamantinoma could not be excluded. On the basis of the roentgen findings and the clinical course, the authors feel justified in regarding this case as one of an adamantinoma arising from the capitate bone.

Four roentgenograms; 2 photomicrographs; 1 diagram.

HAROLD A. SWANSON, M.D.

Calgary General Hospital, Calgary, Alta.

The Deformity of the Medial Tibial Condyle in Nineteen Cases of Gonadal Dysgenesis. Jerzy Kosowicz. *J. Bone & Joint Surg.* 42-A: 600-604, June 1960. (Przybyszewskiego 49, Poznań, Poland)

Gonadal dysgenesis, the result of faulty development in fetal life, occurs (1) in eunuchoids, (2) in patients with numerous congenital anomalies, including short stature, the so-called Turner's syndrome, and (3) in normal-appearing females. One of the most common changes in gonadal dysgenesis is an enlargement and deformity of the medial tibial condyle similar to that found in Blount's disease (tibia vara). This deformity is part of a more generalized process affecting the epiphyseal plates in other bones as well.

Twenty-eight patients with proved gonadal dysgenesis were examined by the author. Four were eunuchoid and 24 had Turner's syndrome. None of the eunuchoid patients exhibited the changes in the medial tibial condyle to be described. Roentgenographically, a deformity of the medial tibial condyle was present in 19 of the 24 patients with Turner's syndrome. Three stages of the deformity were distinguished:

In childhood, the medial portion of the metaphysis either showed protrusion medially or was enlarged in the form of a mushroom. In some cases the medial tibial condyle was slightly depressed. Co-ordinate changes in

the femoral condyles resulted in a flattening of the lateral femoral condyle and a rounded contour and more inferior position of the medial femoral condyle. The tibial epiphyseal plate was altered from its straight and slightly bowed normal contour and became curved inferiorly so that its medial border was depressed. The roentgen diagnosis in the early stages was difficult to make unless alterations in the epiphysis were present in addition to those in the metaphysis.

In adolescence, the changes in the metaphysis were accompanied by closely related alterations in shape of the epiphysis. The medial portion of the epiphysis spread out medially, covering the enlarged metaphysis either partially or completely and, in the latter event, often continued to project inferiorly. In some cases, the fibular heads were situated higher than normal.

In adults, the irregular curvature of the fused epiphyseal line indicated the antecedent stages just described. The medial projection of the tibial condyle often assumed a beak-like shape that varied in size and resembled an exostosis. The other features already mentioned—depression of the medial tibial plateau, flattening of the lateral femoral condyle, superior location of the fibular head, and bony atrophy—were also evident.

Thirteen roentgenograms. PETER TORBEY, M.D.
University of Missouri

Meniscography by van de Berg's Double Contrast Technique. Ulf Zakrisson. *Acta radiol.* 53: 442-448, June 1960. (Centrallasarettet, Linköping, Sweden)

A modification of van de Berg's (1953) double-contrast technic for arthrography of the knee joint is described. This method is intended solely for diagnosing lesions of the meniscus and makes possible detailed examination of the structures.

The joint is aspirated from the medial approach, with as much fluid as possible being drawn off. Then 8 to 10 ml. Umbradil and 20 to 25 ml. air are injected. In adults Umbradil 50 per cent is used (unless the joint is particularly small), and in younger subjects Umbradil 35 per cent. The 50 per cent preparation is also indicated in any case in which some fluid is thought to have been left in the joint. Passive and active movements of the joint are carried out for a few minutes. The patient then lies prone on the table, the foot of which is slightly elevated, and traction is applied to widen the joint space on the side of the meniscus to be examined. Exposures are made within twenty minutes of injection of the medium. Ten tangential projections are obtained under fluoroscopic control during continuous rotation of the joint. The menisci are examined separately. No complications have occurred in 280 such investigations.

In 100 patients in whom surgery was performed, there was good agreement between the roentgen and operative findings. Eighty-two patients not treated surgically were instructed to return if their symptoms recurred; none did so.

In the author's experience, arthrography should be repeated in patients suspected clinically of having a meniscus injury but in whom the initial roentgen examination fails to disclose a lesion.

The value of the direct enlargement of films with the fine-focus tube technic is discussed.

Three serial roentgenograms; 3 photographs; 1 table.

Capt. SAMUEL S. KRICKORIAN, M.C.
Lackland AFB, Texas

Marrow Embolism and Intraosseous Contrast Radiography. Hyman L. Gildenhorn, Vivian B. Gildenhorn, and George Amromin. *J.A.M.A.* 173: 758-760, June 18, 1960. (City of Hope Medical Center, Duarte, Calif.)

A solution of 20 c.c. of Hypaque (diatrizoate sodium, 50 per cent) was injected manually into the marrow cavity of the right femur of a moribund 60-year-old woman with widely metastasizing adenocarcinoma of the colon. It was hoped that a vascular pattern characteristic of the tumor might be demonstrated. The patient expired within twenty-four hours. Postmortem examination showed multiple small emboli consisting of marrow cells in the pulmonary vessels. The largest of the emboli measured 5 mm. in diameter. A spicule of calcified material, about 40 μ in greatest diameter, was found in a pulmonary artery. This is believed to be the first proved instance of marrow embolism incident to intraosseous radiography.

This case, as well as some experimental and clinical studies of injection of infusions and contrast agents into the marrow cavities, emphasizes the potential hazards of the procedure, particularly when fluids are injected with increased pressures produced by mechanical devices.

Two roentgenograms; 2 photomicrographs.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Vascular Patterns in Immobilized, Denervated, or Devascularized Rabbit Limbs. Albert B. Ferguson, Jr., and Yoshihiko Akahoshi. *J. Bone & Joint Surg.* 42-A: 617-624, June 1960. (125 DeSoto St., Pittsburgh 13, Penna.)

By means of an injection technic, the vascular pattern in the hind legs of rabbits was studied roentgenographically in an attempt to clarify some of the physical forces that influence the metabolism of muscle after its immobilization, denervation, or devascularization. The right hind limbs of the animals were immobilized by plaster cast, by cast and skeletal pins, or by internal pin traction of the ankle and knee joints. Denervation, femoral-artery ligation, or tenotomy was done in other animals.

The changes in vascular pattern observed after cast immobilization were dilatation of the main arteries and increased vascularization about knee and ankle joints. After internal fixation alone, similar changes occurred except that there was no dilatation of the main arteries. Increased arborization of small muscle vessels was found after femoral-artery ligation. Diminished vessel size and bizarre vascular patterns were noted after both denervation and tenotomy.

Eleven roentgenograms. PETER TORBEY, M.D.
University of Missouri

THE GENITOURINARY SYSTEM

The Injured Kidney. James F. Glenn and B. Marvin Harvard. *J.A.M.A.* 173: 1189-1195, July 16, 1960. (789 Howard St., New Haven 4, Conn.)

From over 200 cases of suspected kidney injury, 84 proved cases were selected for analysis of diagnostic method, management, and sequelae. Generally, the diagnosis of renal injury depends upon four factors, namely, (1) a history of trauma to the renal area, (2) demonstrable hematuria, (3) positive physical findings, and (4) radiographic evidence. Because other factors

vary widely, classification of renal injury is best made on a radiographic basis. According to the severity of the injury, the 84 patients were divided into four groups: severe, 10 patients; moderate, 20 patients; minimal, 21 patients, and negligible, 33 patients. In 39 of the 84 patients, there was no radiographic evidence of kidney damage.

Five patients in the present series had a plain roentgenogram of the abdomen only; intravenous urography was performed in 66, retrograde pyelography in 20, and cystography in 8.

Evidence of renal injury was apparent on the plain roentgenogram of the abdomen in 11 of 79 patients (flank mass defined 7, psoas shadow obliterated 6, renal outline obscured 3, all three findings, 4). In approximately 50 per cent of the patients undergoing intravenous urography, the findings were positive, including decreased contrast, delay, or nonfunction (15 patients), extravasation of medium (13), incomplete filling of calyx or pelvis (9). The procedure having the greatest percentage of positive findings was retrograde pyelography, with 18 of 20 patients (90 per cent) showing radiographic evidence of renal injury; extravasation was observed in 15, filling defects in 9, and distortion of the calyceal pattern in 8.

Treatment of the patient with renal injury must be individualized and should be governed by the clinical and radiological findings. It is evident from the present study that the great majority of patients require only conservative, supportive measures, including bed rest, blood transfusions, and antibiotics. Hurried emergency exploration of the patient with suspected kidney injury is generally unwise and frequently unnecessary.

Fifty-two patients in the present series were followed for more than two months and 18 for more than one year. Hypertension developed in 3 of 63 patients who were normotensive when first examined. Other late effects of renal injury are fortunately rare but include scarring, infarction, cysts, calcification, hydronephrosis, and persistent infection. Nine of 45 patients had persistent radiographic changes on follow-up.

The authors stress that all patients who sustain renal injury should have periodic examinations for at least a year if late sequelae are to be corrected; these should include appropriate urologic radiography as well as gross and differential renal function studies.

Four tables. JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Renal Fornical Hemorrhages: Their Pathogenesis and Treatment. Anton Pytel. *J. Urol.* 83: 783-789, June 1960. (Urological Clinic, the 2nd Moscow Medical Institute, Moscow, Russia)

In recent years, after an investigation of the fornical apparatus of the kidneys, the urodynamics of the upper ureters, and pyelovenous backflow, it has become possible to detect some interesting physiological and morphological peculiarities of renal disease which throw light on the genesis of profuse renal hemorrhages which were formerly designated "essential."

It has been found that the fornical zone of the calyces is extremely liable to rupture, especially when there is an abnormal elevation of intrapelvic pressure, whether or not a pathological process exists.

In immediate proximity to the fornix lie the major vessels, mostly veins with thin-walled venous sinuses which surround the proximal portions of the calyces

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in the form of a plexus. These venous plexuses are connected with the venae arcuatae as well as with the interlobar veins. When MacMahon and Latorraca (J. Urol. 71: 667, 1954) were studying kidneys removed from 3 patients with so-called essential hematuria, they discovered a communicating canal between the calyx and venous sinuses in the fornical zone. The presence of a venous-calyceal canal leading to hemorrhage was confirmed by the present author *in vivo*.

Six well documented cases are reported, in 5 of which a diagnosis of renal fornical hemorrhage had been suspected from the pyelograms. In 2 cases, Klami's method (addition of hydrogen peroxide to contrast substance) had to be employed to demonstrate the fornical defect. Essentially, the radiologic feature common to all these cases is a horn-like shadow proceeding from the fornical zone of a calyx into the renal parenchyma, considered to represent the communicating canal between the calyx and fornical venous plexuses. Hemorrhages due to this factor can be controlled by renal section, which was performed in 4 of the author's cases.

Curiously, in 12 patients suffering from fornical renal hemorrhage in whom translumbar aortography was performed, the blood supply of the hemorrhagic kidney was more abundant than of the contralateral kidney. Hemorrhages took a more serious course and relapses occurred more frequently in patients with nephroptosis or lumbar dystopia.

A primary cause of fornical hemorrhages, according to the author, is a disturbance of renal hemodynamics and urodynamicism, which in turn is due to disorders of the nerve-muscle tone of the calyces and pelves, together with intermittent lesions of the fornix of the calyx produced by an abrupt elevation of intrapelvic pressure.

Two roentgenograms; 1 photograph; 3 photomicrographs.

ROGER MALTAIS, M.D.
University of Pennsylvania

Compression of the Common Iliac Vessels by Dilatation of the Bladder. Report of a Case. Erik Carlsson and Per Garsten. Acta radiol. 53: 449-453, June 1960. (Karolinska Sjukhuset, Stockholm, Sweden)

To the authors' knowledge, compression of iliac vessels by a distended urinary bladder has not been described in the literature. The case is reported of a 3-week-old infant in whom the distention of the bladder was due to obstruction of its outlet by posterior urethral valves. The circulatory disturbance involved the left lower extremity. The coldness and cyanosis of the leg disappeared following surgical removal of the urethral obstruction.

The circulatory disturbance was reproduced by filling the bladder with 90 c.c. of saline and disappeared when the bladder was emptied.

Femoral venography, with the bladder distended, demonstrated an obstruction of the external and common iliac veins. The right femoral vein filled *via* collaterals below the site of the left iliac obstruction. Repeat venography with the bladder empty was essentially normal.

Close proximity of the iliac vessels to the bladder was thought to be the major factor in the production of vascular obstruction in this case.

Eight roentgenograms.

CAPT. SAMUEL S. KRIKORIAN, M.C.
Lackland AFB, Texas

Calcification of the Vas Deferens in Diabetes. Gordon J. Culver and Joseph Tannenhaus. J. A. M. A. 173: 648-651, June 11, 1960. (100 High St., Buffalo 3, N. Y.)

The authors investigated the frequency and extent of radiographically demonstrable calcifications of the vas deferens and seminal vesicles in 100 adult diabetic males. The relationship of such calcification to the severity and duration of the diabetes and to associated vascular calcifications was also studied.

Of the 100 patients, 11 had calcification of the vas deferens, but this showed no true correlation with duration or severity of the diabetes. Nor was there any correlation between calcification of the vas deferens and of the pelvic arteries.

The roentgenographic appearance of degenerative calcification of the vas deferens and that associated with infection is quite different. The calcification in the authors' cases consisted usually of plaque-like deposits in the walls. The calcification from infection is more intraluminally occlusive and does not involve the wall.

While calcification of the vas deferens is not specific for diabetes, it is highly suggestive.

Three roentgenograms; 1 drawing; 4 tables.

WILLIAM MARTEL, M.D.
University of Michigan

THE ADRENALS

The Roentgen Diagnosis of Adrenal Tumor in Cushing's Syndrome. A. Iannaccone, J. L. Gabrilove, S. A. Brahms, and L. J. Soffer. Arch. Int. Med. 105: 257-263, February 1960. (J. L. G., 79 E. 79th St., New York 21, N. Y.)

This report is concerned with an evaluation of the efficacy of the roentgenogram in making a diagnosis of tumor in Cushing's syndrome. It is based on 57 cases observed by the authors at the Mount Sinai Hospital, New York.

In the patients in this series, the roentgen examination in sequential order included a flat plate, intravenous pyelography, and presacral or perineal gas insufflation, often with concomitant intravenous pyelography and tomography. Air-contrast studies were not made in some patients, either because they were studied prior to the introduction of this technic or because the diagnosis was otherwise apparent. In 52 of the 57 patients the underlying adrenal lesion was proved by exploration or postmortem examination. In the remaining 5, the clinical course following treatment attested to the absence of tumor.

In 9 of 14 cases of adrenocortical carcinoma, the tumor was evident on the flat plate or pyelogram, and in 3 additional patients diagnosis was established by gas insufflation. Two tumors were missed: 1 weighing 100 gm. was removed four months after the roentgen study; 1, in a patient studied prior to the use of gas insufflation, weighed 170 gm. when found at autopsy a year after examination.

There were 9 cases of adenoma in this series. This tumor is ordinarily much smaller than carcinoma and the roentgen demonstration would therefore seem more difficult. In no instance of adenoma was the diagnosis of tumor possible on the basis of a flat plate or intravenous pyelogram, but in 6 a correct diagnosis was made by gas insufflation. No evidence of adrenal tumor was found in the remaining 3 patients even with the aid

of tomography in 2. In all 3 cases, a right-sided tumor was removed six months after the diagnostic study. The adenomas weighed 9.6, 10, and 15 gm.

Thirty-four patients had the nontumorous adrenocortical hyperfunctional form of Cushing's syndrome. In all, a flat plate and intravenous pyelography failed to reveal any signs of tumor. Gas insufflation was utilized in 31 of these patients, and in 24 of this number, tomography was done concomitantly. In 4 patients the procedure was technically unsatisfactory and failed to delineate the adrenals adequately and in another 4—in 2 of whom tomography was employed—an incorrect diagnosis of adrenal tumor was made, probably because of misinterpretation of the adrenal fat pads. In 23 patients, however, the adrenal glands were demonstrated to be normal or slightly and bilaterally enlarged, with no evidence of neoplastic growth, a finding confirmed at operation in 20 and by the long-standing remission induced in the other 3 after pituitary irradiation.

The authors conclude that roentgen examination constitutes a most important method for establishing the presence or absence of adrenal tumor in Cushing's syndrome.

Eight roentgenograms; 5 tables.

TECHNIC

Technical Procedures of Radiodiagnostic Interest. A Symposium. *Brit. J. Radiol.* **33**: 352-361, June 1960.

At the Annual Congress of the British Institute of Radiology, in December 1959, four papers were presented on "Technical Procedures of Radiodiagnostic Interest," abstracts of which follow.

I. The Fundamental Limits of Information Content in Solid State Image Intensifying Panels Compared with Other Intensifying Systems. J. F. Fowler. *Brit. J. Radiol.* **33**: 352-357, June 1960. (Hammer-smith Hospital, London, W.12, England)

For direct viewing, solid state image intensifying panels have the same information content as television systems, and slightly more than electrostatic image intensifiers. The solid state panel works as a storage device because of the slow build-up and decay and is then better than any directly viewed system, including television systems. If, however, television storage systems are used, with magnetic drum or other memory devices, these are slightly better than present solid state panels, the difference in minimum contrast perception of a spot 2 mm. in diameter being the difference between 7 per cent and 5 per cent. For solid state screens three times brighter, these figures would both be 5 per cent. The differences in physical size and shape and in cost and complexity are large, and it appears that the further development of solid state intensifying panels would be worthwhile.

Five figures; 1 table.

AUTHOR'S SUMMARY

II. The Prospects for Solid State Intensifying Screens. S. T. Henderson. *Brit. J. Radiol.* **33**: 357-358, June 1960. (Thorn Electrical Industries, Ltd., Enfield, Middlesex, England)

The author describes a two-layer intensifying screen in which the electroluminescent layer is the source of light and a contiguous cadmium sulfide layer forms the radiation-sensitive part; the latter is made electrically

conductive by the absorption of x-rays. The voltage applied to the electroluminescent layer rises locally, and a bright pattern appears, corresponding to the x-ray pattern. Prototype amplifiers have been developed to give a gain of 50 or more at a dose rate of 1 r per minute.

The slow response time in build-up and decay of the image, due to the properties of cadmium sulfide, prevents the use of the device for moving objects, but the image can be held long enough after the x-ray beam is switched off to permit re-entering the room and inspecting the screen. This image storage effect makes possible several new uses: (1) If made in a very thin form, the amplifier could replace the intensifying screen in a film cassette, making possible reduction of exposures. (2) In surgery where only an occasional x-ray view is necessary, as in the location of foreign bodies, pinning of fractures, and insertion of interstitial radiation sources, examination could be expedited. (3) In radiotherapy with stationary beams the amplifier would be of aid in the necessary alignment.

The problems of reproducibility and control of properties of materials has not yet been fully solved. The author reports that the work is being expanded with radiation-sensitive materials other than cadmium sulfide. Different methods of construction and operation now seem likely to produce even more sensitive designs.

DON E. MATTHIESEN, M.D.
Phoenix, Ariz.

III. A Brief Summary of Industrial Radiography and Automatic Processing. A. J. Weston. *Brit. J. Radiol.* **33**: 358, June 1960.

This paper is not published in full. It is reported that the author described the application of radiographic methods in nondestructive testing for the control of foundry technique and the Elema Automatic Processing Unit. The latter consists of a darkroom, a washing bay, and a drying cabinet. This enables radiographs to be handled at the rate of 80 to 100 per hour, the overall time of a radiograph in the unit being twenty minutes, with the possibility of viewing after nine minutes.

DON E. MATTHIESEN, M.D.
Phoenix, Ariz.

IV. Methods of Multiple Radiography. James McInnes. *Brit. J. Radiol.* **33**: 359-61, June 1960. (Ilford, Ltd., London, W.C. 1, England)

A modification of x-ray techniques is described for obtaining duplicate or triplicate radiographs with a conventional single exposure. Two or three pairs of screens, of different speeds, are incorporated in one cassette. A film is placed within each pair of screens, in 1-2-3 order, so that compensations in speed give uniform exposure to each film. With screens in reverse 2-1 order, the conventional exposure for bone structure will show bone detail in the top film, while the rear, slower-speed screens record a density suitable for soft tissues. The technique is suitable for the investigation of tumors, paraplegia, and exostoses, petrous and mastoid examinations, and studies of the upper and lower ribs and thoracic and lumbar spine.

If the screens are arranged in a 3-1 order, a steeper range of subject opacity results. This arrangement is particularly advantageous in examination for placenta praevia: the exposure necessary for a posterior or low-seated placental site is recorded in the film within the fast screens, No. 3, while the film within the rear No. 1

screens has a reduced exposure level suitable for recording an anteriorly placed placental site.

When the contact radiograph is obtained on nonscreen film, as in radiography of the extremities, employing the 0.3-mm. focal spot, a film between screens can simultaneously be exposed below the table top at the required distance, and a $\times 2$ magnification recorded with the nonscreen exposure. The conventional and magnified radiographs obtained in this way with a single exposure may be usefully compared.

Six roentgenograms. DON E. MATTHIESEN, M.D.
Phoenix, Ariz.

Roentgen Television in Surgery with Special Reference to Stereo-Television. K. Lindblom. *Acta radiol.* 53: 367-370, May 1960. (Karolinska Sjukhuset, Stockholm, Sweden)

The author describes the roentgen television equipment employed in his department for control of surgical procedures. Since 1958 he has been using a Siemens image intensifier and a Fernseh Orthicon television camera fitted with a conventional receiver with satisfactory results. The image is conveyed from the intensifier, through lenses and a mirror, into the camera. The image intensifier can be rotated about an axis passing through the mirror, which permits any desired projection. The method of parallax displacement is used for localization in the third dimension. Recently, the apparatus has been modified for stereo-television. Two roentgen tubes are fitted and are energized alternately at a frequency of 25 c/sec. The two images on the television screen are examined through glasses having perforated disks that rotate synchronously with each beam cycle. The effect is that the two images displayed on the screen of the television tube are seen separately by each eye.

The apparatus has so far been used mainly for localization and removal of renal calculi during pyelotomy. It has been employed also for the removal of ureteric calculi, for the reduction and nailing of fractures, for studying the emptying of the gallbladder and urinary bladder, and for investigating motility during cholangiography and cholegraphy.

The author states that the roentgen load required is about the same as that used in conventional fluoroscopy, the maximum load being 65 kv and 2 ma with a focus-image intensifier distance of 50 cm. The television image obtained is bright and contrast is satisfactory.

Irradiation to the surgeon and his assistant is controlled by avoiding manipulation within the path of the rays and by directing the coned-down beam toward the image intensifier. The danger of secondary radiation is reduced by fitting the primary diaphragm of the roentgen tube with a cone and a lead shield, which is pressed firmly against the patient's body. With a moderately obese patient, the secondary irradiation per minute to the surgeon has been less than 0.001 r to the thorax, abdomen, scrotum, and hand.

Five roentgenograms; 1 photograph.

HAROLD A. SWANSON, M.D.
Calgary General Hospital, Calgary, Alta.

A Stereotaxic Apparatus for Use in Cerebral Surgery. A. M. Hastin Bennett. *Brit. J. Radiol.* 33: 343-351, June 1960. (Isaac Wolfson Foundation, London, England)

The author describes in detail a mechanical device designed to assist in the placing of a long needle or

probe in any predetermined point within the brain through a comparatively small opening in the skull.

The principle underlying the method is simple. The position of the "target" is determined in three mutually perpendicular planes with reference to a rectangular frame of steel tubes fixed horizontally around the patient's head, i.e., the target is found to lie so many centimeters above the rectangle, and so many along its greater and lesser sides. If a sphere is placed so that its center bears the same relation to the rectangle as the target, then a straight line drawn at right angles to the tangent of an arc of the sphere, equal in length to the radius of the sphere, will lie with its end at the target.

By means of movable pointed rods fixed in mountings at the corners of the rectangular frame, the machine is held in place by engaging the points in the outer table of the skull. Calibrations on the mountings permit replacement of the machine in the same position on succeeding occasions if desired. A metal arc bearing a moving clamp attaches to and slides on the sides of the frame and bridges the calvarium superiorly. Through the clamp a long needle can be passed toward any intracranial point, depending upon the position of the clamp on the arc and upon the position of the arc on the frame sides. On the front and one side of the frame, small holders are placed, each carrying an 8-cm. square grid of crossed wires which form 2-mm. squares. A cassette is held in a clip on the frame on the opposite side of the head, the grid being between tube and head. Roentgenograms taken with this arrangement carry the numbered grid markings by means of which intracranial landmarks can be identified. When the double grid lines over the area under investigation are accurately superimposed on the radiograph, it means that the tube has been centered properly and there is no parallax error. It is not possible to align the tube accurately without a telescope, which is lined up with a sight on the frame.

Over 50 operations have been carried out, using the stereotaxic apparatus, some for the implantation of radioactive substances, the majority upon the basal ganglia for Parkinson's disease and allied disorders. When injection is to be made into the basal ganglia, preliminary ventriculography with Myodil is performed for location of intracranial landmarks, followed by injection at the target. In this procedure, the apparatus is used to set the position of two or more guides fastened to the skull. The guides consist of small steel balls, drilled to take the needle as a close sliding fit, held in a base plate pinned to the skull. Surgical complications have been rare and transitory. No operative deaths have been encountered, although one patient died ten days postoperatively from a pulmonary embolism.

Nine roentgenograms; 8 photographs; 1 drawing.
DON E. MATTHIESEN, M.D.
Phoenix, Ariz.

Tonic Muscle Spasms and Blood Pressure Changes Following the Subarachnoid Injection of Contrast Media. An Experimental Study in Dogs with Injection of Kontrast U and Mixtures of Kontrast U and Xylocaine. B. Funkquist and N. Obel. *Acta radiol.* 53: 337-352, May 1960. (Royal Veterinary College, Stockholm, Sweden)

Because of the irritating properties of the water-soluble contrast media, their use in myelography in

human subjects has been limited to the parts of the subarachnoid space which are accessible to spinal anesthesia, *i.e.*, the lumbar portion. Any attempt to adapt the conventional method for the introduction of water-soluble contrast media into the thoracic portion of the subarachnoid space is clearly associated with the risk of the anesthetic agent spreading to the cranial portions of the space during the injection of the medium and producing undesirable effects. It was thought that the short induction time of Xylocaine might offer the possibility of a new approach, in which the anesthetic agent could be dissolved in the contrast solution and thus injected with it. It was also thought that a con-

centration of Xylocaine might be found which would eliminate the irritating effect of the contrast medium without producing any serious vasomotor disturbances.

The authors' experiments demonstrated that in dogs, under light anesthesia and succinylcholine relaxation, myelography of the thoracic part of the spinal cord may be carried out with a mixture of a water-soluble contrast medium (Kontrast U) and Xylocaine provided that the blood pressure is continuously checked and, if necessary, corrected during the procedure.

Nine illustrations, including 1 roentgenogram.

JULIAN O. SALIK, M.D.
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RADIOTHERAPY

Clinical Picture and Prospect of Cure of Malignant Melanoma. Werner Hellriegel. *Strahlentherapie* 111: 510-524, April 1960. (In German) (Universitäts-Röntgeninstitut, Frankfurt/Main, Germany)

In the introduction to his paper, the author presents a long list of skin lesions which show brown coloration, pointing out the difficulty of distinguishing the various pigmented skin tumors and of recognizing malignant melanoma on the basis of the clinical findings.

The radiologist, if he is unable to establish a definite diagnosis, should consult an experienced dermatologist and should use every possible means to avoid biopsy in a patient suspected of having a malignant melanoma. If, however, biopsy seems necessary, it should be performed after x-ray irradiation. Post-irradiation changes do not appear to interfere with a histologic diagnosis. If a later histologic examination should prove that unnecessary radiation therapy has been given, the effect is not as grave as if the patient's life had been endangered by a premature biopsy.

As a further diagnostic tool, radioactive phosphorus is mentioned. P^{32} used as a tracer was found in two or three times higher concentration in malignant melanoma than in the surrounding normal skin. This test, however, is not too reliable.

Malignant melanomas observed during pregnancy usually show a tendency to grow rapidly, particularly when they are located in the breast area. The author prefers radiation therapy to breast amputation. Interruption of pregnancy in no way arrests the growth of the tumor. If metastases are already present, transmission from the mother to the fetus is possible.

Etiologically, not only repeated trauma or irritation but also a single trauma has been found responsible for the development of a malignant melanoma.

The author considers irradiation the treatment of choice for this tumor. Nonradiologists have objected that occasionally this activates the tumor, but such a result was never observed at the institute from which this report comes, in the treatment of either juveniles or adults. Even when metastases are already present, palliative radiation therapy should be attempted, and in many instances it has prolonged life.

The author recommends direct irradiation of the tumor by means of contact therapy, tangential irradiation of the surrounding skin, and treatment of the regional lymph nodes with 200 to 250 kv. After the acute radiation reaction has fully subsided, surgical excision of any residual tumor is recommended. Six to eight weeks at least should elapse before excision is undertaken. The recommended dose is 7,000 to 8,000 r

directly to the tumor, which always leads to an exudative dermatitis. In most instances a considerable or total disappearance of the lesion follows this dosage. If, however, the first series does not bring a complete cure, a second series can be given about two months later, with a dose of 4,000 to 5,000 r. Careful post-irradiation antibiotic therapy and proper skin treatment are, of course, necessary when two series have been administered. Following the second series, a waiting period of several months is recommended before further therapeutic management is attempted, since malignant melanomas quite frequently undergo a very slow involution.

A 54.5 per cent five-year cure rate for melanomas without metastases was obtained at the author's institute, with the method described. For surgical removal and postoperative irradiation of melanomas without metastases, the cure rate was 41.9 per cent.

Eleven photographs; 4 tables.

HERBERT C. POLLACK, M.D.
Chicago, Ill.

Pathology, Diagnosis and Treatment of Liposarcoma. Heinrich Schäfer. *Strahlentherapie* 111: 581-587, April 1960. (In German) (Städt. Krankenanstalten Aachen, Germany)

Liposarcoma is a rare soft-tissue tumor. Three types have been recognized: differentiated, undifferentiated, and round-cell or adenoid. The first group is characterized by infiltrative growth, with rare distant metastasis but frequent local recurrence. The second and third groups are more malignant and show a rapid hematogenous spread.

The clinical symptoms and methods of examination are described. The most important diagnostic procedure is x-ray examination, including soft-tissue films and angiography. A radiograph obtained with special soft-tissue technics permits a distinct delineation of the tumor from the surrounding structures and, at the same time, gives information as to involvement of the bone, which naturally influences the therapeutic management. The importance of a chest film to rule out metastases is also stressed. Erosion of the bone due to pressure by the tumor has been described, but direct osseous invasion by sarcomatous proliferation has never been reported.

The treatment of choice is amputation of a diseased extremity, followed by irradiation. Liposarcomas of the mediastinum and retroperitoneal space are usually highly malignant and are best treated by radical surgery with subsequent x-ray therapy. Indications for ir-

radiation without surgery are acceptable only in case of inoperability, recurrent tumor, or distant metastasis.

A case of a huge lipoma of the thigh with seven recurrences over a period of twenty years and final sarcomatous degeneration is described. X-ray irradiation of the entire thigh was given but did not yield a favorable result.

Three roentgenograms; 1 photomicrograph; 1 table.
HERBERT C. POLLACK, M.D.

Chicago, Ill.

A Histopathological Study on the Prognosis and Radiosensitivity of Retinoblastoma. Isamu Tsukahara. Arch. Ophth. 63: 1005-1008, June 1960. (Faculty of Medicine, Kyoto University, Kyoto, Japan)

In a large series of retinoblastomas, an attempt was made to correlate statistically the histologic characteristics of tumor cells with prognosis and treatment. It was felt that such a study might throw further light on the efficacy of treatment of retinoblastoma of a certain cell type and also on the prognosis.

Eyes with retinoblastoma from 150 patients, examined between 1942 and 1957 at the Institute of Ophthalmology of the Presbyterian Hospital of New York City, were histologically analyzed. Some of the eyes had been enucleated after unsuccessful irradiation (details not given). In retinoblastoma the presence of true rosettes is felt to be an indication of maturity and a high degree of differentiation. Lesions in which rosettes were found to cover more than one-half of the tumor area were classified as well differentiated, and those with only a few rosettes in the periphery of the tumor or with no rosette formation, as less differentiated, or pure retinoblastoma. Tumors in which the development of rosettes was not predominant or in which the area of rosettes comprised less than half of the tumor were designated as mixed. According to this classification, 51 tumors in the present series were considered to be of the well differentiated cell type, 74 of the less differentiated cell type, and 25 of the mixed type.

There was no statistically significant difference in the mortality rate for patients with the less differentiated and the well differentiated tumors. It was found, however, that the mixed type and the less differentiated type resembled each other more closely in terms of mortality and histologic character; if these two types are considered as one group, the mortality is greater than that found in the well differentiated group.

The first two and a half years after the last treatment proved to be the most important period in the follow-up of retinoblastoma patients; of 27 deaths, 22 occurred during that interval.

Diffusion of tumor into the optic nerve constituted the most serious complication of retinoblastoma.

In bilateral retinoblastoma, the degree of differentiation in both eyes can tentatively be considered to be the same.

Well differentiated tumors in this series were the most resistant to x-ray therapy. Irradiation was seen to exert a profound effect upon the character of the tumor cells, often causing a well differentiated tumor to assume the characteristics of one less differentiated.

Five tables.

Epitheliomas of the Maxillary Sinus Treated with External Roentgen Therapy Alone. Results at Five Years. F. Baclesse, A. Ennuyer, and R. Calle. J. de

radiol. et d'électrol. 41: 368-375, June-July 1960. (In French) (Fondation Curie, Paris, France)

Observations on 94 cases of epithelioma of the maxillary sinus and of the ethmoido-maxillary region, treated at the Curie Foundation from 1923 to 1953 with external roentgen therapy alone, lead the authors to stress the importance of the radiographic study of the tumor (tomography and roentgenography of the base of the skull) in classifying the different varieties and thus adding to the classical division into carcinomas of the infrastructure and of the suprastructure.

Clinical and radiographic classification on this basis shows the importance of the extension of the carcinoma and of its site in the prognosis. Forty-four cases in this series involved the infrastructure and 19 the suprastructure.

The "limited" carcinomas of the infrastructure showed excellent results (6 cures in 7 cases treated). The "extended" cases gave 6 survivals out of 37 treated patients. The carcinomas of the suprastructure produced 4 survivals for 19 cases. Among the remaining 31 cases there were only 3 survivals. This group included 11 pansinusal, 16 ethmoidomaxillary, and 4 unclassified carcinomas.

Roentgen therapy was given through fixed fields, 180 to 200 kv, 1 mm. Cu, 50 to 60 cm. distance. The localizing light beam was used, affording good ocular protection.

RENÉ HOURI, M.D.

New York, N. Y.

Technic of Irradiation of Epitheliomas of the Tonsil by Combined External High-Energy Roentgen Therapy (Betatron, 22 Mev) and Interstitial Curie Therapy (Au-198 Wires). Application of the Concept of Two-Volume-Targets. B. Pierquin and M. Gasiorowski. J. de radiol. et d'électrol. 41: 375-380, June-July 1960. (In French) (Institut Gustave-Roussy, Centre clinique et thérapeutique, Villejuif, Paris, France)

The irradiation of epidermoid carcinomas of the tonsil with a combination of external roentgen therapy and interstitial curietherapy (radium) has produced superior statistical results. Ennuyer has shown that the five-year survival rate averages 30 per cent when the combined method is used and only 15 per cent with a single method (Ennuyer and Batani: Les tumeurs de l'amygdale et de la région vélopalatine. Paris, Masson et Cie, 1956).

The authors describe a new technic combining high energy roentgen therapy (22 Mev) to a large volume target, followed by interstitial therapy with Au-198 wires to a small volume target (tumor residuals).

Precision centering is accomplished by transverse tomography.

Eleven illustrations.

RENÉ HOURI, M.D.

New York, N. Y.

Preoperative Irradiation for Cancer of the Esophagus. Eugene E. Clifton, John T. Goodner, and Eugene Bronstein. Cancer 13: 37-45, January-February 1960. (Memorial Center for Cancer and Allied Diseases, New York, N. Y.).

Of a total of 119 patients with carcinoma of the esophagus seen between July 1, 1956, and Dec. 31, 1958, 20 were included in a series to receive preoperative irradiation and subsequent surgical exploration. In 11 of these, resection was performed and the tumor was found to have regressed markedly as a result of the radiation therapy. The extent of both the primary dis-

ease and the lymph-node metastases was limited. In contrast, in 13 patients who had immediate exploratory operations, the cancer was resectable in only 5, and in every case the disease was extensive. In still another group of 6 patients who received preoperative radiation therapy but not under optimal conditions, 3 (50 per cent) had resectable cancer but again the disease was more extensive than in those patients with planned preoperative irradiation. It should also be noted that in those patients who did not have exploratory operation at the optimal time, approximately six weeks post-irradiation, there might be rapid progression and a return of obstruction even though there was excellent response to irradiation.

There were 2 immediate postoperative deaths among the group of patients receiving preoperative irradiation; 1 from staphylococcal pneumonia and coronary occlusion and 1 from acute pancreatitis, the result of an error in surgical judgment when an aneurysm of the pancreatic artery was removed at the time of the esophagostomy. This last patient was a poor risk from the beginning.

Four case reports are given: 2 illustrating recovery following preoperative irradiation and surgery two years eight months and eight months after operation; 1 of three months recovery after resection alone; 1 of a man who refused post-irradiation surgery at the optimal time because of a feeling of well-being but returned two months later, when the tumor was adherent to the upper lobe of the left lung, the trachea, and the great vessels. He died four and a half months after operation.

Eleven roentgenograms; 5 photographs.

The Combined Radio-Surgical Treatment of Carcinoma of the Cervix Uteri. G. R. Kurrle. J. Coll. Radiologists Australasia 4: 44-49, June 1960. (Peter MacCallum Clinic, Melbourne, Australia)

The results of "combined radiosurgical treatment" of carcinoma of the cervix (1950-54) at the Royal Women's Hospital and Peter MacCallum Clinic, Melbourne, are presented.

Although the radiotherapy technic has been modified since 1950, basically it is the Paris six-day, single insertion intracavity method, with radon instead of radium. Resulting dosage to Manchester Point A ranges from 6,000 to 6,290 gamma r in six days. A special applicator has been designed, which consists of two permanently paired Lucite ovoids into which radon tubes can be inserted; it has a flat Lucite handle, which allows easier and more consistent positioning of the radon sources. Packing the rectum away from the radioactive source is also easier and the rectal dose is lower. In many cases the radon application was followed by deep x-ray therapy to the pelvic lymph node areas, using a six-port technic, with central shielding, for 3,000 to 3,500 r (tumor dose?) in four weeks. Over the last few years there has been a strong tendency to omit this part of the treatment. Surgery was ordinarily undertaken six to eight weeks after completion of radiotherapy, but on occasion up to six months elapsed. The only contraindications to surgery appear to have been extrapelvic or local bony disease, provided the patient's general condition was satisfactory and there was some movement on bimanual examination in the general mass of tumor tissue in the pelvis. Surgical procedures were of the Wertheim type, with radical node resection.

For those patients in whom complete combined therapy, as outlined above, was possible, the results in the various stages compare very favorably with the results reported by others: Stage I: 26 five-year survivors from 33 patients (79 per cent); Stage II: 30 five-year survivors from 45 patients (67 per cent). There were only 6 patients with Stage III cervical carcinomas; 3 were alive at the end of five years. [The various survival figures when applied to all patients seen, i.e., the absolute cure rate, are not so good, particularly for Stage III cases, where only 3 of 31 patients (9.6 per cent) were salvaged.—J.W.B.]

Some important data have been gathered with respect to the survival rate in the presence of residual cervical tumor and/or metastatic pelvic nodes. Of 87 patients, 29 were found at operation to have involved nodes, residual tumor, or both, following irradiation; of this number, 13 (44.8 per cent) survived five years, indicating that they were indeed salvaged by surgery.

As to that part of the treatment consisting of external deep x-ray therapy, one must weigh the greater morbidity and the delay in time of operation on the one hand against the favorable effect of such irradiation on local disease and involved lymph nodes, both strongly indicated in the current study. [For not very clear reasons, the author appears to favor dropping the external deep x-ray therapy.—J.W.B.]

Morbidity for the combined method of treatment is a little high with respect to complications (fistulae in 7 of 87 patients, or 8 per cent). Minor complications are not tabulated.

The author concludes that results with their combined radiosurgical procedure are comparable to those with other methods for Stage I cases and definitely better for Stage II. It is admitted that the degree of morbidity and the prolongation of treatment are unfavorable aspects. Currently under study is the feasibility of employing megavoltage external therapy alone or combined with radical surgery.

Two photographs; 11 tables.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

The Sensitization Response in Patients with Cancer of the Uterine Cervix. John B. Graham and Ruth M. Graham. Cancer 13: 5-14, January-February 1960. (Roswell Park Memorial Institute, Buffalo, N. Y.)

Some patients with cancer of the cervix have basal cells with dense basophilic, finely vacuolated cytoplasm in the vaginal smear before any treatment. These cells come from the parabasal layer of the non-malignant squamous epithelium of the cervix and vagina. When a fair proportion, i.e., 10 per cent or more of the desquamated nonmalignant epithelial cells are of this type, there is usually a favorable response to radiotherapy and the patient is said to have a good sensitization response (SR).

In a study of 147 patients receiving radiotherapy, the overall five-year cure rate for 54 with a good SR (over 10 per cent) was 69 per cent, while that for 93 patients with a poor SR (less than 9 per cent) was 18 per cent. The SR is most accurate in Stages II and III; the maximum difference in results with good and poor sensitization rates was seen in Stage IIA, where 10 of 11 patients (91 per cent) with good SR were alive and well five years after radiotherapy, as compared to 2 of 10 patients with poor SR. When treatment was by radical hysterectomy, the cure rate was higher in those

with poor SR, 69 per cent as compared with 43 per cent with good SR.

The technic for obtaining the smears is described in detail. It is simple, but, for that very reason, every aspect of it must be done correctly if reproducible results are to be obtained. SR is lowered by biopsies, repeated physical examination, and pelvic infection but seems to be higher in postmenopausal and older patients.

The sensitization and radiation responses correlate rather closely in the prognosis of cervical cancer. The radiation response is characterized by changes in the normal epithelial cells of the vaginal smear during radiotherapy (Surg., Gynec. & Obst. 84: 153; 166, 1947. Abst. in Radiology 50: 141, 1948). In an unselected series of patients at the Roswell Park Memorial Institute, Buffalo, N.Y., treated with radiotherapy alone, 45 of 53 patients with poor SR subsequently showed a poor radiation response, while in 34 of 39 with marked SR a good radiation response was subsequently obtained. This gives an agreement of 86 per cent.

It is believed that in the sensitization response we have a change in the normal cells that presages a favorable response of the tumor to irradiation and an unfavorable result if surgery is applied. This is a phenomenon of practical and theoretical importance, presenting a method of rational selection for the mode of treatment. As an index of host resistance, the SR may afford some insight into the manner in which cancer is healed with the help of irradiation.

Four figures; 9 tables.

Contribution to the Problem of Diagnosis, Treatment and Prognosis of Wilms Tumor. Alexander J. Chilkot. J. Urol. 83: 804-812, June 1960. (1040 Park Ave., New York 28, N. Y.)

In the early 1930's, the author became interested in the treatment of those patients with Wilms' tumor who, for any reason, could not be subjected to operation and were therefore referred to the radiologist for palliative treatment. Previous experience had demonstrated that, with the usual program of radiotherapy, the tumor was likely to reduce in size rapidly, but would recur at a later date. In an attempt to destroy the more resistant cells, as well as the very radiosensitive portions of the neoplasm, it was decided to administer small but frequent doses of irradiation over a long treatment time. Two cases of inoperable Wilms' tumor receiving such protracted radiotherapy are reported; no mention is made of other patients similarly treated.

The first patient was a 14-month-old boy who was seen in August 1934, with a huge right-sided Wilms' tumor, considered inoperable because of its size and adhesions. For treatment, a 200-kvp apparatus was employed with h.v.l. of 0.9 and 1.4 mm. Cu. Alternately, anterior and posterior portals were treated daily in increments of 116 r (air), until 1,000 r had been delivered to each area. The dose increment was then reduced to 76 r, with two days of rest between treatments, until an additional 1,000 r had been delivered to each area. In similar manner, three-, four-, five-, and finally six-day intervals were allowed between treatments until a total air dose of 5,000 r per area was reached. The estimated total tumor dose was 7,110 r, delivered in 122 treatments over twenty-two months. In the years that followed, the boy did well, with

normal growth and development. In 1946, however, hematuria suddenly developed and the right kidney was removed. Other than a dilated pelvis and thickened capsule, there was no residual renal substance. However, nests of definite embryonal Wilms' tumor cells could be identified; these were surrounded by sclerosed renal capsule. The patient's recovery from the operation was uneventful. At the time of the report he was twenty-six years of age, physically and mentally well, and with no evidence of metastasis.

The second patient, a four-and-a-half-year-old girl, was seen in October 1938, with a huge tumor which filled the right abdomen. No biopsy was attempted, but the author believes the appearance and response were typical of Wilms' tumor. The treatment plan was similar to that employed in the first case, with slight modifications. Three treatment areas were used, with half-value layers of 1.4 and 1.9 mm. Cu. The dose increment for the first month was 135 r (air), and afterward 90 r, until a total air dose per area of 3,000 r had been delivered in fourteen months. The total tumor dose was 6,334 r. Because viable tumor cells had been found in the kidney of the first patient ten years after irradiation, the right kidney was removed from the second patient also. No evidence of tumor was detected in the specimen.

Both patients are well more than twenty years after the discovery of an inoperable Wilms' tumor. Both have a slight degree of underdevelopment of the abdominal musculature on the treated side and slight scoliosis. The second patient also had an underdevelopment of the lower right thoracic cage and slight skin damage. She has given birth to two normal children.

The author believes that radiotherapy should not be employed alone in the treatment of inoperable Wilms' tumor, but should, in due time, be followed by nephrectomy.

Two photographs.

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Experimental Haemopoietic Replacement. Possible Use in Radiotherapy. Peter Ilbery. J. Coll. Radiologists Australasia 4: 50-54, June 1960. (University of Sydney, N. S. W., Australia)

The author describes briefly experimental developments in radiation protection and the treatment of murine leukemia in relation to the feasibility of application of radiotherapy at the present time. The paper is largely a summary of experimental and clinical data reported by others. To date it would appear that following massive whole-body irradiation in man, efforts to repopulate marrow by means of homologous bone-marrow grafting have been unsuccessful because the immunological reaction between host and donor transplant has not been overcome. For the time being it would seem more feasible to extend the range of radio- and chemotherapy by concentrating on autologous bone-marrow grafting. Recent improvements in very low temperature ($-80^{\circ}\text{C}.$) techniques for storage of bone-marrow aspirates seem promising. The efficacy of remission marrow seems dubious but awaits trial. Technical advances in delivery of a uniform dose in radiotherapy are not expected to change the position greatly. Needed is a better understanding of the biological mechanisms of tissue grafting and carcinogenesis.

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RADIOISOTOPES

The Treatment of Toxic Nodular Goiter with Radioactive Iodine: 10 Years' Experience with 436 Cases. Milton Eller, Solomon Silver, Stephen B. Yohalem, and Robert L. Segal. *Ann. Int. Med.* 52: 976-1013, May 1960. (S.S., 35 E. 85th St., New York 28, N. Y.)

A sharp divergence of opinion exists as to whether the toxic nodular thyroid should be treated with radioactive iodine or by surgical extirpation. Advocates of surgical resection are influenced by fear of a possible association of cancer with toxic nodular goiter and a belief that the response to radioiodine is poor. In the Thyroid Clinic of the Mount Sinai Hospital (New York), it is thought that the incidence of cancer in toxic nodular goiter is so low that the risk in treatment with I^{131} is not great. Furthermore, the authors have found that these goiters respond well to radioactive iodine.

The method of treatment and calculation of dosage in hyperthyroid patients have been discussed in detail elsewhere (see, for example, Quimby, Feitelberg, and Silver: *Radioisotopes in Clinical Practice*, 1958). The dose administered is based on microcuries retained per gram of estimated thyroid weight. A single dose calculated to deliver about 8,000 rads is given, and two to three months are allowed to elapse for its full therapeutic effect to become apparent before further treatment is considered. The average number of treatments per patient in any given series of cases depends to a large extent upon the size of the initial dose. Where there is an attempt to get a high percentage of cures with one dose, in general there will be fewer total treatments and higher initial doses, but a higher percentage of post-therapeutic myxedema. The authors prefer to use smaller doses, to treat again and more often if necessary, and to avoid the post-treatment hypothyroidism as far as is possible.

In a total series of 1,603 hyperthyroid patients, 436 with toxic nodular goiter were treated with I^{131} ; this group included 127 patients with solitary nodules. Treatment was instituted in the first year after the occurrence of toxic symptoms in 35 to 40 per cent of all patients, regardless of the type of involvement—nodular or diffuse.

In 92 per cent (354 of 384) of the evaluated cases of toxic nodular goiter, the patient became euthyroid under treatment with I^{131} ; in 7.8 per cent (30 patients) permanent myxedema developed. The percentages were almost identical for diffuse toxic glands. The incidence of permanent myxedema was slightly higher following the treatment of solitary toxic nodules (10.7 per cent), but this sequel was not encountered with substernal thyroids. All of this series of thyrotoxic patients had their hyperthyroidism controlled with I^{131} alone.

About 40 per cent of the nodular and 50 per cent of the diffuse toxic thyroids were cured with a single dose of I^{131} . The patients with Graves' disease averaged 1.9 treatments each, while those with toxic nodular goiters averaged 2.2 treatments each. Patients with toxic nodular goiters required an average total administered dose of 10.3 mc of I^{131} to produce a remission of the hyperthyroidism; those with Graves' disease needed 7.2 mc. This represents differences in uptake and size of gland rather than radiosensitivity. The toxic nodular goiters averaged 53 gm. in weight before treatment and 37 gm. after treatment. The ability of a toxic nodular goiter to pick up radioactive

iodine was only moderately less than that of a toxic diffuse goiter.

Solitary nodules in hyperthyroid patients responded well to treatment with I^{131} . Substernal thyroids, even very large ones, may be treated successfully with radioiodine; pressure symptoms due to goiter are not a contraindication to I^{131} therapy.

Thirty-two per cent of the patients with Graves' disease and 18 per cent of those with toxic nodular goiters exhibited exophthalmos in some degree. After treatment with radioactive iodine, eye signs improved but did not disappear.

Eighty per cent of all patients had pulse rates in excess of 100 per minute before treatment; relieving the hyperthyroidism with I^{131} relieved most of the tachycardias. Auricular fibrillation was found in 25 per cent of the patients with toxic nodular goiters and in 10 per cent of those with Graves' disease; after I^{131} therapy, one-half to three-fourths of those who had fibrillation had a regular rhythm. Before treatment with I^{131} , one-fourth of the patients with toxic nodular goiters showed some degree of congestive heart failure, as did 10 per cent of those with Graves' disease; after therapy, a marked improvement was apparent in the decompensated patients. Patients with angina pectoris were also benefited by I^{131} therapy.

Diabetes mellitus associated with hyperthyroidism lessened in severity when the hyperthyroidism was relieved with I^{131} .

Twenty tables.

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Effect of Methylthiouracil and Iodide on the Iodinated Constituents of Thyroid Tissue in Graves' Disease. E. Yamazaki, A. Noguchi, and D. Ward Slingerland. *J. Clin. Endocrinol.* 20: 889-893, June 1960. (D. W. S., Boston VA Hospital, Boston, Mass.)

The distribution of radioiodine among the various iodinated constituents of thyroid tissue was determined chromatographically in patients with Graves' disease who had been treated with methylthiouracil for twenty days and then with iodide alone for ten days before thyroidectomy. Specimens of normal tissue from euthyroid patients with adenoma of the thyroid were used as controls. In the tissue from patients with hyperthyroidism the proportion of inorganic radioiodide was higher (28.2 per cent) than normal (8.1 per cent) and the ratio of radiomonoiodotyrosine to radiodiiodotyrosine was higher (2.2) than normal (0.68). The latter could be explained in most instances by a block in iodine organization leading to a deficiency of iodine for the formation of diiodotyrosine. In 2 hyperthyroid patients, however, there was no apparent block in the organization of iodine. This block in the conversion of monoiodotyrosine to diiodotyrosine in the hyperthyroid human subject might have been the result of iodide therapy, but it seems more probable that it was a long-lasting effect of methylthiouracil.

Two tables.

AUTHORS' ABSTRACT

Defective Iodination of Tyrosine a Cause of Nodular Goiter? John C. Floyd, Jr., William H. Beierwaltes, Vernon N. Dodson, and Edward A. Carr, Jr. *J. Clin. Endocrinol.* 20: 881-888, June 1960. (University Medical Center, Ann Arbor, Mich.)

Twenty patients with colloid nodular goiter, 7

patients with Hashimoto's struma, and 15 patients without thyroid disease (all non-deaf) were tested with radioactive iodine and potassium thiocyanate for a thyroidal defect in iodination of tyrosine. In the cases of colloid nodular goiter with a family history of goiter there was a higher incidence and more severe degree of defective iodination of tyrosine than in the cases of colloid nodular goiter without a family history of goiter. Defective iodination of tyrosine was demonstrated in one sibling with proved colloid nodular goiter and one with Hashimoto's struma. Iodination of tyrosine was impaired in a patient with her fourth recurrence of colloid nodular goiter. These data suggest that defective iodination of tyrosine is not uncommon in euthyroid non-deaf subjects with colloid nodular goiter, and may occur on a familial basis.

Two figures; 1 table.

AUTHORS' ABSTRACT

Effect of Salt Feeding on Thyroid Metabolism of I^{131} in the Dog. Joseph B. Boatman, Marvin J. Rabinovitz, and John M. Walsh. *Am. J. Physiol.* **198**: 1251-1254, June 1960. (Allegheny General Hospital, Pittsburgh, Penna.)

Five per cent by dry weight of sodium chloride was added to the diet of 6 adult male dogs, while the diet of a control group remained unchanged. After twelve weeks, the 24-hour I^{131} uptake, PBI^{131} , serum and urine sodium and potassium were measured. Two weeks later, five-hour Na^{24} and I^{131} -thyroxine dilution curves were determined from serial blood samples in the anesthetized animals. The salt-fed dogs had elevated 24-hour I^{131} uptake and PBI^{131} , decreased serum sodium and increased serum potassium, and both the total urine sodium and potassium were increased with salt feeding at twelve weeks. In the salt-fed dog, both Na^{24} and I^{131} -thyroxine dilution volumes were increased at five hours over the values for the control group, indicating expansion of extravascular volume. It was suggested that alterations of I^{131} metabolism were influenced by extrarenal factors of expanded fluid volume and tissue concentration of electrolytes in addition to the dominant factor of renal electrolyte regulation with salt loading.

Five figures.

AUTHORS' ABSTRACT

The Action of Various Goitrogens in Inhibiting Localization of Radioiodine in the Thyroid and Thymus Glands of Larval Tree Toads. W. Gardner Lynn and James Norman Dent. *Biol. Bull.* **118**: 430-438, June 1960. (W. G. L., Catholic University of America, Washington 17, D. C.)

Tadpoles of *Hyla versicolor* collected near Oak Ridge, Tenn., were immersed for fifteen days in spring water containing phenylthiourea, $KClO_3$, $KSCN$, $KClO_4$, or KIO_3 , followed by a twenty-four-hour immersion in 20 μ c/ml of I^{131} , a thyroid-destroying dose. When treatment with any one of these drugs was continued during the period of I^{131} administration, radiation damage to the thyroid was prevented. The inhibitory effect of $KClO_4$ on the thyroid persisted even when treatment was discontinued two days before immersion in the I^{131} solution. The effects of phenylthiourea and $KSCN$ were dissipated more quickly, since the thyroid showed extensive damage when treatment was stopped immediately before I^{131} administration and complete destruction when it was stopped two days before.

In control animals, the thyroid-destroying dose of I^{131} extensively damaged the thymus gland as well. Of

the drugs tested, only $KClO_4$ sufficiently inhibited the I^{131} uptake by the thymus to prevent damage, and only when it was present during the period of exposure to I^{131} .

Although phenylthiourea was protective to the thyroid, it proved to be completely without protective value to the thymus. None of the drugs provided any protection for the thymus if their use was discontinued before I^{131} administration. This lesser degree of effectiveness for the thymus may indicate that this gland is damaged by lower radiation levels than is the thyroid.

Eleven figures; 1 table.

I^{131} -Labeled Fat and Pancreatin as a Differential Absorption Test in Patients with Steatorrhea. Abraham A. Polachek and Robert F. Williard. *Ann. Int. Med.* **52**: 1195-1200, June 1960. (VA Hospital, Fort Howard Division, Baltimore 18, Md.)

It has been shown that patients with steatorrhea, whether due to pancreatic insufficiency or malabsorption syndrome, have low blood I^{131} levels after a fat meal with radioiodinated triolein. The two conditions may be differentiated by giving an additional meal of the labeled hydrolysis product of fat, radioiodinated oleic acid, normal blood I^{131} levels then being obtained in the group with pancreatic disease. The use of pancreatic extract along with I^{131} -labeled fat suggested itself as a more physiologic test to differentiate steatorrhea due to pancreatic insufficiency from that due to malabsorption syndrome.

Seven patients with calcific pancreatitis, 6 of whom also had diabetes mellitus, and 7 with various types of malabsorption syndrome were studied by plasma radioactivity determinations after I^{131} -labeled fat meals without, and later with, concomitant pancreatic extract (Viokase) administration. Six of the 7 patients with calcific pancreatitis had markedly increased fat digestion and absorption after pancreatic extract administration. The pancreatic extract had no appreciable effect in improving fat absorption in the 7 patients with malabsorption syndrome. In the patients with chronic pancreatitis there was a rise of the mean maximal plasma I^{131} from 3.4 to 9.8 per cent with pancreatic extract, while in the malabsorption group the change was only from 6.0 to 6.4 per cent.

Besides its use as a physiologic test to differentiate patients with pancreatic insufficiency from those with absorptive difficulties, the method is also valuable in assessing the effect of pancreatic extract as substitution therapy in the individual patient with chronic pancreatitis.

Four graphs. CHARLES M. GREENWALD, M.D.
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I^{131} Triolein Tolerance Curves in Patients with Diabetes Mellitus. Their Similarity to Those Observed in Myocardial Infarction. Herschel Sandberg, Byong Sok Min, Leonard Feinberg, and Samuel Bellet. With the Technical Assistance of Jean Schraeder. *Arch. Int. Med.* **105**: 866-872, June 1960. (Philadelphia General Hospital, Philadelphia 4, Penna.)

I^{131} triolein tolerance curves were studied in 27 patients with diabetes mellitus. The patients were divided into two major groups: those between nineteen and fifty-nine years of age (19 cases) and those sixty to eighty-six years old (8 cases). Those in Group I were subdivided into diabetics with demonstrable athero-

sclerotic cardiovascular complications and those without. The peripheral vascular complications were manifested by intermittent claudication, atherosclerosis obliterans, and in most instances one or more amputations. The criteria employed for the diagnosis of atherosclerotic heart disease are those recommended by the American Heart Association.

In patients under sixty with demonstrable evidence of atherosclerotic complications, abnormal curves, as shown by peak values for elevated whole-blood activity and circulating lipoprotein activity, as well as elevated 24-hour whole-blood and circulating lipoprotein activity, were obtained, almost identical with those in a previously reported myocardial infarction group (Seller *et al.* *Am. J. Med.* **27**: 231, 1959. *Abst. in Radiology* **75**: 167, 1960). Lesser degrees of abnormality were found in diabetics under sixty with no clinically demonstrable evidence of atherosclerotic complications.

In patients over sixty years of age the I^{131} tolerance curves were similar to but slightly lower than those of the normal controls. The duration of insulin administration had no direct correlation with an abnormal tolerance curve, but in diabetics taking large daily doses of insulin, higher radioactivity was shown in the post-prandial blood samples.

Four figures; 3 tables.

Accidental Acute Irradiation from Cobalt-60. G. A. Elliott. *South African M. J.* **34**: 524-529, June 18, 1960. (University of the Witwatersrand, Johannesburg, Union of South Africa)

The accidental exposure of a traffic policeman in the Transvaal to a radioactive cobalt-60 source on Dec. 1, 1959, received considerable publicity in the press. The author was the clinician in charge of the case, believed to be the first of the sort in South Africa, from the fifth day after exposure. The dosage was not known until Dec. 10, when, according to official report, the local skin dose was considered to be 900 r, the gonadal dose 37 r, and the total-body dose 2.5 r.

At no time were there symptoms or signs of the acute radiation syndrome, but from Dec. 4 to Dec. 8 there was an urticaria-like eruption 12 inches below the left iliac crest. Observations were made on the patient as if he had been subjected to a body dose significant in the sense that it might at least temporarily affect the bone marrow. Apart from a transient leukocytosis, no abnormalities were found. On March 8, 1960, the blood picture was normal. A specimen of seminal fluid at this time showed a marked reduction in the number of spermatozoa and a reduced proportion of motile forms. These findings could be compatible with a radiation effect but could equally well be due to a number of other causes. The gonadal dose at its worst was well under the doubling mutation rate dose.

After a press interview on Dec. 8, subsequent reporting of the case was both accurate and sympathetic. The importance of (1) managing the psychological aspects and of (2) keeping the public informed, particularly through the press, is discussed.

One graph.

Blood Loss During Adenoidectomy and Tonsillectomy Measured with Radioisotopes. R. L. Ruggles. *Ann. Otol., Rhin. & Laryng.* **69**: 360-374, June 1960. (St. Luke's Hospital, Cleveland, Ohio)

Three methods of measuring blood loss during adenoidectomy and tonsillectomy are described in detail:

(1) studies with radioactive chromium; (2) injection of radioactive iodinated serum albumin (Risa); (3) gross measurement of the blood in sponges and suction bottles. These three methods were employed and the results correlated in 17 patients.

It was found that the chromium method was too inaccurate to be used with the small amounts of blood lost in this procedure. The accuracy of the Risa method as compared with the gross method varied from a difference percentage of 3 to 32, with an average of 12 per cent. The average blood loss was 12.1 per cent of the total volume, with a range of 4 to 20 per cent.

The Risa method has practical value in following the course of a surgical problem in which blood loss is a factor and may be used in unusual cases where a large amount of blood is expected to be lost. For the usual adenoidectomy and tonsillectomy, however, it becomes rather cumbersome unless enough trained personnel are available and the veins of the patient are large and sturdy enough to withstand a minimum of 4 venipunctures. Where continual loss of blood is suspected, the daily volume may be followed with greater accuracy with the Risa method than with the hematocrit readings in common use. Accuracy, as well as radiation hazard, increases with larger amounts of Risa injected.

Four photographs; 1 table.

P^{32} Localization of Malignant Melanoma of the Posterior Choroid. J. O'Rourke and Eleanor Collins. *Arch. Ophth.* **63**: 801-811, May 1960. (3800 Reservoir Rd., N.W., Washington 7, D.C.)

While it has been established that melanomas of the choroid do concentrate increased amounts of radiophosphorus, attempts to detect tumors of the posterior choroid with the P^{32} uptake test, with the technique employed for anterior tumors, have not been successful. The authors compare the results of tranconjunctival and transscleral counting methods, first on the basis of total radioactivity measured, and second, with respect to their accuracy in locating the tumor site.

Radiophosphorus uptake measurements were made in 7 patients with proved malignant melanoma of the posterior choroid and in 1 with subretinal hemorrhage. Counts were performed with the patient under general anesthesia. The following results were obtained:

1. With 8 tranconjunctival countings, the posterior choroid melanoma was localized correctly in only 1 instance and the average focal increase of activity was only 25.3 per cent above the mean.

2. With 6 transscleral countings, the tumor was localized correctly in all instances, and the average focal increase in radioactivity was 74 per cent.

3. Tumors having a mass of more than 300 c. mm. and those having high epithelioid cell content took up greater amounts of P^{32} than did small tumors and those of predominantly spindle-cell composition.

4. There was no apparent correlation between P^{32} uptake and factors of pigmentation, vascularization, or necrosis.

The following criteria are proposed for the detection of posterior choroid tumors:

1. Anterior and posterior quadrant counts of one minute each to be done on the suspect eye, under general anesthesia, allowing adequate rotation of the globe for anterior (tranconjunctival) counting and necessary surgical exposure, including detachment of the appropriate rectus muscle, for posterior (transscleral) counting.

2. A positive result of P^{32} uptake for posterior tumor to be based on a total posterior count exceeding the anterior value by more than 40 per cent, and radioactivity detected over the tumor site exceeding the mean of posterior counts by more than 40 per cent. The locus of highest posterior radioactivity and the site of solid detachment should correspond.

The overall advantage of posterior counting performed in the manner described seems to be, first, that total emissions counted per minute are greater, thereby reducing the chances of error, and second, that actual localization of the tumor site is more accurate.

Six figures; 1 table.

The Technical Procedure in Kidney Examinations with Radioactive Isotopes. N.-E. Säterborg. *Acta radiol.* 53: 433-441, June 1960. (Serafimerlasarettet, Stockholm, Sweden)

The author has used radioactive iodopyracet in the

evaluation of renal function in 24 cases. Scintillation counter methods were employed, and emphasis is placed upon the size of the aperture of the counter and accurate centering. On the basis of his experience, the author doubts that radioactive isotopes will have any particular future clinical significance in examinations of the kidneys, as in the majority of cases the procedure provides no information additional to that obtainable by other means. It is of some value when satisfactory contrast density in the renal pelvis is not achieved at urography and when there is some uncertainty as to whether this is due to pathologic changes and reduced renal function or to a faulty technic.

In an editorial note following this paper, attention is called to the confusion in the use of the terms "renogram" and "nephrogram." These terms will not be employed in *Acta radiologica* to indicate the excretion curve of an isotope through the kidney.

Eight figures.

RADIATION EFFECTS

Further Observations on Late Radiation Necrosis Following Therapy of Skin Cancer. The Results of Fractionation of the Total Dose. H. L. Traenkle and Dattatreya Mulay. *Arch. Dermat.* 81: 908-913, June 1960. (468 Delaware Ave., Buffalo 2, N. Y.)

In 1955, one of the authors (H. L. T.) reported a study of 55 instances of late radiation necrosis occurring among 935 cases of basal- and squamous-cell cancer of the skin treated by roentgen therapy at the Roswell Park Memorial Institute (Buffalo, N. Y.) between 1946 and 1953 (*Arch. Dermat.* 72: 446, 1955. *Abst. in Radiology* 67: 924, 1956). In this series the irradiation was administered in 1,000 r fractions, for either 4,000 r in an overall treatment time of eight to ten days or 5,000 r in ten to twelve days. The incidence of radiation necrosis in this previously reported series is now compared with that in another series of 816 cases of skin cancer treated (from 1950 to 1955 inclusive) with daily fractions of 500 r, 400 r, and 300 r, over a slightly more prolonged treatment time. Ten cases of radiation necrosis were discovered in the second series.

In each series, the overall time and total dose combinations were consistent with optimum dosage as indicated on time-dose plots in general usage throughout the world. When the total dosage employed in each series is converted to an equivalent biologic cumulated dose by the formula $D_0 = D_T/F_T$, the effective cumulated dose for each scheme of treatment is within the range ordinarily considered optimum.

The time of onset, the duration, course, and seasonal distribution of occurrence of the episodes of necrosis were the same in the two series.

When calculated by the life-table technic over a four and one-half year period, the probability of late necrosis developing in the second series treated with smaller fractions is less than 3 per cent as contrasted with almost 14 per cent in the previously recorded series.

As far as normal tissue tolerance is concerned, it appears that when fraction doses as high as 1,000 r are employed, the reliability of the time-dose curves is impaired. Therefore, it is erroneous to assume that all points along the curve are valid without regard to the degree of fractionation of the total dose.

Irrespective of the overall time of the irradiation,

the size of the individual fraction doses may be a more important factor than formerly realized.

Three figures; 3 tables.

The Influence of X-Ray Contact Therapy of Hemangiomas on the Growing Skeleton. Jaromir Kolár and Václav Bek. *Strahlentherapie* 111: 561-573, April 1960. (In German) (Radiologische Klinik der Universität Prague, Czechoslovakia)

Results are reported of follow-up examinations six to thirteen years after x-ray contact therapy (50 kv) of 760 hemangiomas. The radiation was administered with consideration of its effect and influence on the growth of bones. It was found that this method of irradiation is by no means harmless to the growing bones, as is still asserted occasionally.

Changes in the irradiated bones were found in 9 per cent of the children, particularly on the superficially located epiphyses, such as those of the hand, wrist, knee, and elbow.

The localization and nature of the bone changes, the age of the patients, and the radiation technic were correlated. The changes consisted of osteoporosis, often associated with sclerosis. In advanced cases, marked hypoplasia and even radiation necrosis occurred. In a few instances, small exostoses were found in the treated area.

Since growing bones are most sensitive to irradiation, osseous changes were observed in the irradiated area even when the overlying skin appeared normal.

The authors conclude that accurate information about the effect of x-ray contact therapy on growing bones can be obtained only if the clinical and cosmetic check-up is combined with careful x-ray studies of the underlying skeleton. On the basis of their experiences, they arrived at the conclusion that x-ray contact therapy in children, at 50 to 60 kv, in the region of the superficially located epiphyses should be avoided. In other regions, a single dose should not exceed 150 r and a series of treatments should not go beyond 600 to 700 r to the skin. The number of treatment series should be limited to two.

Four roentgenograms; 4 tables.

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The Role of X-Ray Therapy to the Neck Region in the Production of Thyroid Cancer in Young People. A Report of Thirty-Seven Cases. E. Hunter Wilson and Samuel P. Asper, Jr. *Arch. Int. Med.* 105: 244-251, February 1960. (601 N. Broadway, Baltimore 5, Md.)

From 1933 to the time of this report, 37 patients with carcinoma of the thyroid who were twenty-five years of age or less were seen at the Johns Hopkins Hospital, Baltimore, Md. Thirteen were males and 24 females; 34 Caucasians and 3 Negroes. The diagnosis of thyroid cancer was established histologically following surgical removal in all. In 16 patients (43 per cent) there was a history of irradiation to the head, neck, or chest, for such conditions as thymic enlargement, acne, chronic tonsillitis, hemangioma, laryngeal polyps, and enlarged tongue. Eighteen of the 37 patients were seventeen years of age or younger at the time of the operative diagnosis of cancer, and 19 were eighteen or over. In this arbitrary grouping, 13 (72 per cent) of the 18 in the younger series had had irradiation; 3 (16 per cent) of the older age group gave such a history.

These data indicate a significantly higher incidence of preceding irradiation in children with thyroid cancer than in the general hospital population and support the concept that x-ray therapy is a causative factor in the development of thyroid cancer in young persons.

Abstracts of the records of the patients with and without previous irradiation are included, in two tables.

Myocardial Injury from Therapeutic Irradiation. Mary Catterall and William Evans. *Brit. Heart J.* 22: 168-174, April 1960. (London Hospital, London, England)

In patients who undergo radiotherapy for malignant neoplasms in the region of the chest, the diagnosis of cardiac infarction has sometimes been entertained when chest pain has appeared as a prominent symptom during or after irradiation. Twenty-six patients were studied with electrocardiograms before and after treatment to determine whether incidental irradiation of the heart can cause electrocardiographic changes which simulate those found in cardiac infarction. The group included 6 patients with inoperable carcinoma of the bronchus and 8 women with carcinoma of the right breast and 12 with carcinoma of the left breast who had undergone mastectomy. In all save 3 patients, clinical, electrocardiographic, and radiologic examination showed no abnormal signs in the cardio-arterial system. In 1 patient with systemic hypertension, the electrocardiogram demonstrated left ventricular preponderance and fluoroscopy revealed some enlargement of the left ventricle. In 2 patients the electrocardiographic findings suggested the presence of limited and painless coronary arterial disease.

The 6 patients with carcinoma of the bronchus received a radical course of irradiation from a telecobalt-60 unit, for a total dose of 4,000 rads. The 20 patients with carcinoma of the breast were given deep x-ray therapy from 250-kv machines directed to the chest wall and the lymphatic drainage areas, for a total of 3,650 r.

In the 6 patients with inoperable bronchial cancer and in the 8 with cancer of the right breast, in all of whom the path of the therapeutic rays did not traverse any critical portion of the heart, the electrocardiogram taken after irradiation was found to be unaltered from the tracing taken before.

Among the 12 patients who had undergone radio-

therapy following mastectomy for carcinoma of the left breast, electrocardiographic changes limited to the T waves were found in 9. The changes appeared within four months of the completion of treatment, rarely earlier than this. They lasted for a period of nine months and had disappeared entirely within twelve months in each of the 5 patients followed for that period of time. These findings indicate that the myocardial lesions resolved completely and without scarring, emphasizing the innocent nature of the injury to the heart. This temporary injury seems inevitable when therapeutic irradiation of high dosage is applied in such close proximity to the heart. In the 3 patients in whom irradiation had not affected the electrocardiogram, marker films showed that the heart was so placed in relation to the path of the rays that it lay outside the geometrical edge of the beam.

The importance of the findings lies in the recognition of the cause of the electrocardiographic changes. In the patient who has undergone radiotherapy of the left chest during the previous twelve months and who presents with chest pain, any electrocardiographic changes which may be demonstrated are more likely to be due to the effects of irradiation than the result of cardiac infarction.

Four roentgenograms; 3 electrocardiographic tracings. WENDELL M. BURNS, M.D.
Covina, Calif.

Leukemia Following X-Ray Therapy for Ankylosing Spondylitis. Donald C. Graham. *Arch. Int. Med.* 105: 51-59, January 1960. (Dept. of Medicine, University of Toronto, Toronto, Ont., Canada)

In this report the case histories of 5 patients who died of rapidly progressive acute myeloid leukemia following x-ray therapy for ankylosing spondylitis are presented. The interval between initial roentgen treatment and the diagnosis of leukemia in these cases ranged from eight months to eight and a half years, with an average of five years, five months; that between the last roentgen treatment and diagnosis of leukemia ranged from one month to eight and a half years, averaging three years, nine months.

Between 1945 and June 1958 at the arthritis unit of the Department of Veterans' Affairs hospitals in Toronto, the diagnosis of ankylosing spondylitis was recorded in 591 patients, 146 of whom had been treated by x-irradiation. There were 4 leukemia deaths among the 146 irradiated patients, and to date there have been no cases of leukemia among the 445 who received no radiation. This difference in leukemia incidence between the irradiated and nonirradiated groups is highly significant statistically.

The mechanism of leukemogenesis following radiation exposure is unknown. It is probable that radiation injury of hematopoietic tissue is but one of several complex factors concerned. It has been demonstrated that the risk of leukemia increases with the size of radiation dose absorbed by the hematopoietic marrow and with the number of courses of x-ray therapy administered. While this hazard is greater at high dose levels it still exists, though in lesser degree, at lower levels of radiation exposure. No consistent "pre-leukemic" changes have been recognized to date among spondylitic patients treated by x-irradiation.

While this potential hazard of x-ray therapy for ankylosing spondylitis should be recognized and

weighed against the probability of concrete benefit to patients so treated, the evidence available at present scarcely indicates that the risk is sufficient to warrant complete discontinuation of this form of treatment. Careful hematologic studies should be carried out at frequent intervals during the course of roentgen therapy and any evidence of hematopoietic injury, even slight leukopenia, should probably contraindicate further irradiation. Repetition of courses of roentgen therapy should be avoided except in patients with severe painful disability who fail to respond to other therapeutic measures.

Geographical Variation in Leukaemia Mortality in Relation to Background Radiation and Other Factors.

W. M. Court Brown, R. Doll, F. W. Spiers, B. J. Duffy, and M. J. McHugh. *Brit. M. J.* 1: 1753-1759, June 11, 1960. (W. M. C. B., Western General Hospital, Edinburgh, Scotland)

There is no doubt that the risk of developing leukemia can be increased by exposure to ionizing radiations, but it is not clear whether this effect is produced by all types of exposure or whether it is limited to certain levels of dose and of dose rate. Doses given at very low rates may be presumed to produce mutations in marrow cells comparable to the gene mutations in germ cells, and if such mutations are capable of playing any part in the development of cancer, the possibility would have to be considered that the natural background radiation might also be responsible for some cases of leukemia. It is difficult to make direct observation of the effect of background radiation, because any effect is likely to be small in comparison with that due to other causes. Populations of the order of hundreds of thousands would have to be studied, and it is hard to maintain the same standards of diagnosis through such large groups.

With these misgivings in mind, the authors made measurements of background radiation in four areas of Scotland—in two predominantly granite districts (Aberdeen City and Aberdeen County) and in two districts of sedimentary rocks (Edinburgh and Dundee). In all four areas, most of the houses and buildings are made of local stone, so that a sufficient homogeneity exists to give significance to mean population dose-rate. Measurements of gamma-ray dose rate were made out-of-doors and in houses, with a portable high-pressure ionization chamber having the required sensitivity and long-term stability. The cosmic ray response of the instrument, corrected to allow for overhead shielding, was subtracted from the reading at each site before application of an appropriate gamma-ray calibration factor to derive the local gamma ray dose rate. Cosmic rays and potassium 40 contribute most of the dose from natural sources, additional to the local gamma radiation. The incidence of leukemia in each of the areas was also determined.

The highest mortality from leukemia (146 per cent of the expected) was recorded in Aberdeen, the second highest (124 per cent of the expected) in Edinburgh, and the lowest (87 per cent of the expected) in Glasgow. Estimates of the mortality attributed to acute leukemia, chronic myeloid leukemia, and chronic lymphatic leukemia show that the excess mortality in Aberdeen was principally due to a high mortality from the two former types, while that in Edinburgh was principally due to a high mortality from chronic

lymphatic leukemia. The excess in Aberdeen and Edinburgh cannot reasonably be attributed to random fluctuation. Possible explanations include: better case finding, high economic status, and exposure to radiation. The reasons for the higher mortality from leukemia in wealthier strata is unknown; it may be no more than a reflection of better case finding and, perhaps, a greater exposure to ionizing radiation.

Local differences in the average exposure to diagnostic radiography may be greater than differences in background radiation. They may contribute to the variation in leukemia mortality but are unlikely to be a major factor in its production.

It has been estimated that a dose of 1 rad to the bone marrow might result in the production of about one case of leukemia per million man-years for perhaps ten years from the date of exposure. On this basis, the observed differences in bone-marrow dose would be unlikely to produce more than one or two cases per million persons in ten years. In contrast, the difference between Aberdeen and Dundee in the mortality from acute leukemia and chronic leukemia in a similar period is calculated to have been of the order of 170 cases per million persons and the difference between Aberdeen and Edinburgh to have been of the order of 130 cases per million persons. In the authors' opinion, therefore, the finding of an excess mortality in Aberdeen from two types of leukemia that are known to be produced by radiation cannot be attributed to the high level of the background radiation.

Whether the assumptions made in the present study are justified will not be apparent until further data are available. It is, however, clear that it is insufficient to study leukemia mortality only in relation to background radiations. Proper interpretation of geographical variations can be made only when the effect of social and economic factors can also be assessed.

Four figures; 7 tables. PETER TORBEY, M.D.
University of Missouri

Prompt Effects of High-Level Irradiation on Animal Metabolism. James P. Ellis, Jr., Robert T. Clark, Jr., Walter A. Rambach, and John E. Pickering. *Am. J. Physiol.* 198: 1245-1250, June 1960. (USAF Aerospace Medical Center (ATC), Brooks Air Force Base, Texas)

Blood acid-base related components and free amino acids in plasma, spinal fluid, and five tissues were measured in Rhesus monkeys exposed to whole-body gamma irradiation from a Ba^{140} - La^{140} source, in doses of 500 to 30,000 r. Samples collected two hours later showed an increased acidity in the blood. There was a rise in blood lactic acid but no consistent change was found in blood pyruvate. A correlation of these findings with reductions in the arterial CO_2 tension and plasma CO_2 content indicated that the metabolic acidosis was greater than the respiratory alkalosis resulting from increased pulmonary ventilation. Two-dimensional chromatograms revealed that plasma glucose was reduced and plasma uric acid was increased. The altered levels were related to the postirradiation interval and the total dose. The free amino acid content of the plasma was increased in proportion to the dose. Of the seven amino acids detected in the spinal fluid, an elevated glutamine level was the only consistent change.

Sixteen chromatograms; 4 tables.

AUTHORS' ABSTRACT

The Effects of Experimental X-Radiation on the Cornea. Frederick C. Blodi. Arch. Ophthalm. 63: 20-29, January 1960. (State University of Iowa, Iowa City, Iowa)

A study was made of the late effects of x-irradiation on the cornea of the rat, under conditions as close as practicable to those usually employed in radiotherapy. The possibility of preventing or alleviating corneal damage by the administration of cysteine before the irradiation was also explored. Animals were divided into four groups, with a control (or controls) in each group. The bodies were shielded with lead with the exception of the head.

Group I: Four rats were given 300, 400, 500, and 600 r, respectively, at weekly intervals, for eight weeks, for a total of 2,400, 3,200, 4,000, and 4,800 r. The right eye was enucleated five weeks and the left eye nine weeks after the last treatment.

Group II: Four rats received 700, 800, 900, and 1,000 r, respectively, at weekly intervals for eight weeks, for a total of 5,600, 6,400, 7,200, and 8,000 r. The right eye was enucleated eleven and the left eye fourteen weeks after the last treatment.

Group III: The irradiation was the same as in Group II. Immediately before each x-ray treatment, 8 of the 10 animals received a retrobulbar injection of 0.2 c.c. of a 5 per cent cysteine solution on the right side. In 2 control animals an isotonic saline solution was injected retrobulbarly. All eyes were enucleated twelve weeks after the last irradiation.

Group IV: The irradiation was again the same as in Group II, but the cysteine was injected intraperitoneally, in a 20 per cent solution, 80 mg. cysteine per kilogram of body weight. The animals were killed ten weeks after the last irradiation.

No definite histologic changes could be found in the cornea in animals receiving less than 800 r per session. Severe corneal damage was apparent only when more than 900 r per session was administered. These corneas showed a severe stromal edema, and perforation occurred when the x-ray dosage reached 1,000 r per session. In all these eyes corneal metachromasia disappeared. When 800 r was given per session, corneal metaplasia was only partially destroyed; corneal vascularization and lymphocytic infiltration were a frequent finding.

The changes in the epithelium were minimal. The initial epithelial damage seemed to disappear and the healing process was apparently complete.

The clinical assumption that the late corneal damage by irradiation affects mainly the stroma was corroborated by the author's experiments. A thinning of the corneal fibers, edema, loss of metachromasia, and finally necrosis with perforation was demonstrated.

The retrobulbar injection of cysteine failed to protect the cornea against the x-ray lesions, while intraperitoneal injection of cysteine provided almost complete protection against late corneal damage.

Seven figures.

Acute Radiation Effects in the Esophagus. F. Lamont Jennings and Anne Arden. Arch. Path. 69: 407-412, April 1960. (Department of Pathology, University of Chicago, Chicago 37, Ill.)

A study was made of esophageal changes occurring in rats subjected to 3,000 r x-irradiation to the thorax, with shielding of the remainder of the body. The dose of irradiation administered approximates that com-

monly used in thoracic radiotherapy. These studies indicate that the esophageal epithelium is significantly radiosensitive. Within six days mucosal necrosis was apparent, with loss of the superficial epithelium. By the seventh day there was extensive sloughing of the necrotic esophageal mucosa; this sloughing resulted in plugging of the esophagus with debris, which appeared to reach a maximum at about ten days, and esophageal dilatation. By the twelfth day there was accumulation of inflammatory exudate, in addition to the necrotic debris, in the esophageal lumen, with moderate chronic submucosal inflammation. These acute changes parallel to some degree those observed by Seaman and Ackerman in human beings (Radiology 68: 531, 1957), and the period of esophageal mucosal erosion in the experimental animals corresponds to the period of dysphagia and substernal burning commonly experienced by patients after thoracic radiotherapy. Healing of the mucosa occurred fairly promptly and re-epithelialization appeared to proceed rapidly during the third postirradiation week. Submucosal fibrosis and telangiectasia were conspicuous after epithelial restoration and persisted as permanent radiation sequelae. Esophageal diverticula, with herniation of the mucosa through a defect in the esophageal muscularis, were common late complications of radiation esophagitis. Nine photomicrographs.

Cortisone and Irradiation. II. Pulmonary Necrosis and Blood Vessel Impairment in Irradiated Cortisone-Treated Rat Lung. Charles C. Berdjis. Dis. of Chest 37: 621-626, June 1960. (Fort Detrick, Maryland)

The histopathology of the effect of cortisone on the irradiated rat lung has been discussed previously (Dis. of Chest 32: 481, 1957. Abst. in Radiology 71: 473, 1958). In the investigation described here, cortisone was given to irradiated and nonirradiated rats to determine whether this pharmacological agent is responsible for the necrosis, hemorrhage, and vascular impairment found so frequently.

Forty healthy young adult rats were given 3 mg. of cortisone acetate daily for a period of one hundred days. Twenty rats from this group also received a dose of 3,000 r x-irradiation to the chest three days after administration of cortisone. A third group of 20 untreated and nonirradiated rats served as controls. A fourth group of 20 rats received only 3,000 r to the chest. The animals were kept under observation for one hundred days.

Results: Control Animals: The lungs of the control animals showed essentially no pathologic change. The irradiated lung of noncortisone treated rats displayed a patchy or lobular atelectasis with acute, subacute, or chronic inflammation, producing either pneumonitis, bronchopneumonia, bronchitis, or bronchiectasis with peribronchial and parenchymal abscesses. More or less extensive peribronchial, perivascular, and alveolar fibrosis was present in all cases. The bronchi were partly or entirely collapsed or obliterated, disclosing partial resorption. In the irradiated lung of cortisone treated rats, atelectasis was partly or entirely replaced by "liquefaction" or necrosis, accompanied by hyperemia, stasis, intense congestion, or hemorrhage. The lung parenchyma suffered from necrosis and hyperemia, leading to frequent extravasation and/or hemorrhage. Most of the lungs of nonirradiated cortisone-treated rats revealed hyperemia, congestion, hemorrhage, and patchy atelectasis with multiple necrosis similar to

that described previously as liquefaction. The alveolar walls also exhibited occluded capillaries, while the small arteries showed evidence of narrowing of the lumen and thickening of the wall. The findings were similar to those described for irradiated lung of cortisone-treated rats. The large branches of the pulmonary artery, especially near and at the main trunk, showed a thickened wall and a narrowing lumen. The media disclosed proliferation with foci of mucoid degeneration and/or calcification resembling the Mönckeberg type of arteriosclerosis.

The author concludes that, although cortisone inhibits the inflammatory reaction and reduces the amount of lymphoid tissue and the production of fibrosis, it appears to be responsible for liquefaction, necrosis, and blood vessel impairment. Irradiation reinforces the injurious effects of cortisone at the level of the lung parenchyma. Cortisone seems to act as a hemorrhagic agent *per se*.

Eleven photomicrographs.

JOHN P. FOTOPoulos, M.D.
Northwestern University Medical School

Cortisone and Radiation. III. Histopathology of the Effect of Cortisone on the Irradiated Rat Kidney. Charles C. Berdjis. Arch. Path. 69: 431-439, April 1960. (Fort Detrick, Md.)

In previous studies (Dis. of Chest 32: 481, 1957. Abstr. in Radiology 71: 475, 1958), it was found that cortisone may modify the course of histopathologic reaction of lung parenchyma of irradiated rats. The present experiments were conducted to ascertain the effects of cortisone on the irradiated rat kidney.

Two groups of young rats received 3×500 r of x-radiation to both kidneys. One-half of these animals were given 3 mg. of cortisone daily for a period of one hundred days. A third group received only cortisone, and a fourth group, untreated and nonirradiated, served as the control. While the kidneys in the control rats showed no alterations, glomerulosclerosis was found in the cortisone-treated animals, with intercapillary thickening, capillary thrombosis, hyaline masses, and cystic formations. These lesions were more marked in the irradiated groups.

Irradiation seemed to reinforce the injurious effect of cortisone in the kidney by affecting especially the glomerular and vascular system.

The action of cortisone upon the kidney appeared to be elective in the glomerular tufts and the blood vessels.

Arteriosclerosis and arteriolonephrosclerosis were outstanding findings in the irradiated cortisone-treated rat kidney.

Fat particles were present in some glomeruli of the cortisone-treated, but in none of the irradiated animals. The presence of fat and tinctorial affinities of the glomerular lesions and their interrelationship with some specific lesions (diabetes and lupus erythematosus) are discussed.

Eleven photomicrographs.

Acute Tubular and Glomerular Lesions in Rat Kidneys After Uranium Injury. Sergio A. Bencosme, Robert S. Stone, Harrison Latta, and Sidney C. Madson. Arch. Path. 69: 470-476, April 1960. (S. C. M., University of California Medical Center, Los Angeles 24, Calif.)

This is a report of changes seen by light microscopy

in rat kidneys after acute uranium injury. Uranium nitrate hexahydrate was injected subcutaneously as a 0.6 per cent solution in saline. A dose of 14.4 mg./kg. was found suitable for producing extensive renal lesions. It was given to 26 rats; 18 rats received an equal volume of saline, and 6 were untreated.

The glomerular and tubular changes were correlated with polyuria and proteinuria occurring in these animals. The most striking change was a large centrolobular lesion developing in all glomeruli after the third day. This lesion was composed of fibers staining like collagen. Basement membranes adjacent to small lesions sometimes showed varying amounts of PAS (periodic acid-Schiff)-positive material. The formation of collagen in the centrolobular area suggests the existence of an intercapillary cell different from endothelial cells.

The glomeruli of uranium-treated animals also exhibited vacuolation and hyaline droplets in epithelial cells. The capsular space contained hyaline droplets, large globules, and an amorphous material.

Marked changes in the tubules, such as necrosis, regeneration, hyaline droplets, and casts, were similar to those described by others. The increase of cytoplasmic bodies in proximal convoluted tubules while casts became less prominent suggests that these bodies may be formed by resorption of material from the lumen of the tubules.

Six photomicrographs; 1 table.

Effects of X-Irradiation on Embryos at Critical Stages of Heart Development. W. M. Copenhaver, Rhoda H. Van Dyke, and Roberts Rugh. Yale J. Biol. & Med. 32: 421-430, June 1960. (College of Physicians and Surgeons, Columbia University, New York 32, N. Y.)

Previous studies on embryonic and larval amphibians have indicated that cardiac muscle is relatively radioresistant. These studies, however, did not deal with the effects of x-irradiation at specific stages of cardiac development. The authors therefore undertook an investigation to determine the effects of irradiating embryos at successive stages of cardiac differentiation.

Embryos of the salamander *Ambystoma punctatum* were irradiated at Harrison's stages 26, 30, and 34. These are critical stages of heart differentiation ranging from the time when the primordial endocardial cells separate from splanchnic mesoderm to the time when the heart attains a tubular form and begins to contract. X-ray exposures ranged from 100 to 10,000 r. Following irradiation, the embryos were reared at a temperature of 12 to 13° C.; nonirradiated controls were kept at the same temperature.

In general, the amount of development retardation was proportional to the total amount of irradiation and inversely proportional to the degree of differentiation at the time of exposure. In all of the series studied, there was a latent period between exposure to irradiation and the appearance of developmental defects. The embryonic central nervous system and eyes were particularly radiosensitive. Microcephaly developed in a high percentage of embryos exposed at early stages.

Cardiovascular anomalies occurred in all embryos exposed to 250 r or above at stage 26, and in all embryos exposed to 500 r or above at stages 30 and 34. With high doses, differentiation was so retarded that circulation never developed in the embryos. With intermediate doses, circulation developed for a period, only

to fail subsequently. It is of interest that the pulsation rate remained approximately normal for a considerable period after the magnitude of contraction had decreased.

For previous articles by Rugh on the effect of irradiation on the fetal eye and nervous system, the reader is referred to *Radiology* **71**: 729, 1958, and *Arch. Ophthalm.* **54**: 351, 1955 (Abst. in *Radiology* **67**: 155, 1956).

Twelve figures; 1 table.

SYDNEY F. THOMAS, M.D.
Palo Alto, Calif.

Studies on Susceptibility to Infection Following Ionizing Radiation. V. Comparison of Intraperitoneal and Intravenous Challenge at Intervals Following Different Doses of X-Radiation. C. Phillip Miller, Carolyn W. Hammond, and Sonia K. Anderle. *J. Exper. Med.* **111**: 773-784, June 1, 1960. (Department of Medicine, University of Chicago, Chicago 37, Ill.)

Ten-week-old female CF-1 mice were subjected to a single total-body exposure of x-radiation in one of the following doses: 300, 400, and 500 r. At intervals thereafter, susceptibility to bacterial infection was determined by intraperitoneal challenge with graded inocula of *Pseudomonas aeruginosa*. Mice exposed to 400 or 500 r were also challenged by intravenous inoculation.

The LD 50 of the test microorganism in each challenge was estimated from the mortality data.

Exposure to 300 r caused little increase in susceptibility to this experimental infection. Four hundred roentgens caused a moderate increase on the third day post-irradiation with return to normal on the seventeenth. Leukocyte counts (geometric means) following this dose of radiation did not fall below 1,200. Five hundred roentgens caused a marked increase in susceptibility which lasted from the third to eleventh day, during which period the leukocyte counts were below 800. On the twentieth day, susceptibility to infection was normal, although the geometric mean of leukocyte counts was only 2,200.

Comparison of mortalities resulting from equivalent inocula introduced by the two routes (intravenous and intraperitoneal) showed no difference in unirradiated mice. However, among mice irradiated with 400 or 500 r, higher mortalities resulted from intravenous inoculation. The difference was found to be due to the establishment of a small focus of infection at the site of intravenous injection as a result of leakage of a minute fraction of inoculum into the perivenous tissues of the tail. Bacterial multiplication occurred in such foci in irradiated (leukopenic) mice, but not in unirradiated mice, nor at the site of intraperitoneal inoculation even in irradiated mice.

Five figures; 4 tables.

AUTHORS' SUMMARY

Shortening of the Life Span of Mice by Irradiation with X-rays and Treatment with Radiomimetic Chemicals. Peter Alexander and Dorothea I. Connell. *Radiation Res.* **12**: 38-48, January 1960. (Chester Beatty Research Institute, Royal Cancer Hospital, London, England)

An impressive number of observations have shown that exposure of animals to a large whole-body dose of radiation (i.e., more than 100 r) shortens the life span even if no deaths occur within several months after irradiation. The magnitude of this effect depends very

largely on the way the dose is administered, as fractionation greatly reduces it. Whether small doses, insufficient to produce any immediate symptoms, reduce life span by a small amount or whether there is a threshold below which no change is seen is not known.

The authors have studied the effect on the life span of mice of irradiation and certain radiomimetic compounds. The findings were as follows:

The life span of CBA mice was greatly reduced by exposure to 600 r, 1,100 r, and 1,300 r of x-rays given in two to four sessions three weeks apart.

The resistance to further x-irradiation of these heavily irradiated animals was not reduced. The single acute lethal dose (i.e., LD 50/30) was unchanged so long as more than three weeks were allowed to intervene between the last sublethal dose and the test dose used to determine the LD 50.

The irradiation does not hasten typical changes seen in unirradiated aging animals, such as alterations in collagen and the appearance of a liver lesion. The few facts so far available do not indicate that the process is similar to spontaneous aging.

Cytotoxic chemical substances (nitrogen mustard, Chlorambucil, Myleran) can also, under suitable conditions, produce a shortening of the life span. Experiments are under way to determine if this effect is due to the production of somatic mutations or is due to destruction of cells. Preliminary observations indicate that the latter mechanism is more probable.

Five figures; 2 tables.

Mutation as a Cause of Death in Offspring of Irradiated Rats. J. F. McGregor, A. P. James, and H. B. Newcombe. *Radiation Res.* **12**: 61-66, January 1960. (Atomic Energy of Canada Ltd., Chalk River, Ont., Canada)

X-irradiation of the germ cells of male rodents is known not only to reduce the litter size of the first-generation progeny but also to increase the frequency of stillbirths and to reduce the life span of live-born offspring. The authors describe an attempt to obtain a quantitative assessment of the relative contributions of direct and indirect genetic components in x-ray-induced early deaths.

The reproductive tissues (testes, epididymides, and vasa deferentia) of 90-day-old male rats were exposed to 800 r of 2,000-kvp x-rays at a rate of approximately 200 r/min. The bodies of the animals were shielded. The incidence of infant death (stillbirth and death up to weaning) was studied in litters sired by these irradiated rats. Litters were conceived throughout a twenty-four-day period after irradiation. In the entire experiment, 64 irradiated males sired 70 litters, and 348 unirradiated males sired 281 litters.

The offspring of irradiated fathers were much more prone to infant death than were those of unirradiated fathers; the difference was highly significant as indicated by a chi-square test. In the irradiated group, of 331 young, 140 died (42.3 per cent); in the nonirradiated group, of 2,576 young, 667 died (25.9 per cent).

The major cause of increased infant death in combined litters from conceptions at all times following irradiation was found to be indirectly genetic, i.e., a result of reduced litter size. A significant increase in death among litters conceived at five to eight days after irradiation, however, could be attributed to direct genetic causes.

Four figures; 3 tables.

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X-Irradiation Lethality Aggravated by Sexual Activity of Male Mice. Roberts Rugh and Erica Grupp. *Am. J. Physiol.* 198: 1352-1354, June 1960. (Radiological Research Laboratory, Columbia University, New York 32, N. Y.)

Sixty CF₁ mice were given 600 r whole-body x-irradiation, a dose calculated to kill 30 per cent of the animals in thirty days. Half of the mice were isolated as controls and the remaining half were provided with an adequate number of nonpregnant, mature females for daily matings for the next thirty days. The controls showed 33 per cent lethality while the animals in the second group, aggravated by frequent sexual activity, showed 73 per cent lethality. Sexual activity more than doubled the lethal effect of 600 r x-rays. Litters derived from irradiated, sexually active males mated during the first week, resulted in an average of 3.1; matings during the second week produced an average of 2.7 (normal control size 9.6). Matings during weeks three to seven were sterile. Fertility was recovered by some animals at eight weeks (litter size, 6.9) and by some as late as seventy-five days. Control irradiated males, after resumption of fertility, produced litters of 7.3.

One graph.

AUTHORS' ABSTRACT

Studies on Radiation-Induced Mammary Gland Neoplasia in the Rat. I. The Role of the Ovary in the Neoplastic Response of the Breast Tissue to Total- or Partial-Body X-Irradiation. E. P. Cronkite, C. J. Shellabarger, V. P. Bond, and S. W. Lippincott. *Radiation Res.* 12: 81-93, January 1960. (Brookhaven National Laboratory, Upton, N. Y.)

In the experiments described here, total-body exposure of 40-day-old female Sprague-Dawley rats to 400 r of 250-kvp x-rays delivered in a single dose was followed by a 79 per cent tumor incidence, with one or more neoplasms of the breast at the end of ten months post-exposure. The incidence of breast neoplasms in nonexposed rats of the same age was 2 per cent. The overall incidence of nonbreast tissue neoplasms was 2 per cent and distributed in all groups with and without radiation exposure.

Exteriorizing and shielding the ovaries, or transplanting nonexposed ovaries into ovariectomized irradiated rats, or shielding the head did not reduce the incidence of breast neoplasms below 69 per cent. Shielding the ovarian area reduced the incidence slightly, to 40 per cent. Removal of the ovaries before or after total-body irradiation reduced, but did not eliminate, neoplasia of the breast in 19 to 23 per cent. A further reduction to 25 per cent occurred when the exposure was delayed to one hundred and twenty days of age, although this group was studied for only six months post-exposure. Exposure of the ovaries alone, ovariectomy, or sham ovariectomy did not induce neoplasia of the breast.

These results were interpreted to mean that total-body irradiation or exposure of all of the animal except the ovaries or the head induces breast tumors. The presence of functioning ovary is required for the maximum neoplastic response of the breast to irradiation. It is believed that 400 r of total-body irradiation both hastens the onset of neoplasia of the breast and induces a higher incidence than would be expected to occur if the nonexposed rats were allowed to live out their life span.

The histologic types of neoplasms of the breast were,

in decreasing order of occurrence, adenofibroma, adenocarcinoma, fibroadenoma, and fibrosarcoma. When multiple neoplasms were found in the same animal, the neoplasms were usually of the same type. Although the adenocarcinomas were observed to appear somewhat earlier and the adenofibromas somewhat later, no further correlation of histologic type with any radiation, shielding, or surgical treatment was found.

The relatively short period of time between exposure and the development of a high incidence of breast neoplasms suggests that the young female Sprague-Dawley rat offers many advantages in studies of neoplasia induction by total-body irradiation.

Two figures; 1 table.

Studies on Radiation-Induced Mammary Gland Neoplasia in the Rat. II. The Response of Castrate and Intact Male Rats to 400 r of Total-Body Irradiation. C. J. Shellabarger, S. W. Lippincott, E. P. Cronkite, and V. P. Bond. *Radiation Res.* 12: 94-102, January 1960. (Brookhaven National Laboratory, Upton, N. Y.)

Male Sprague-Dawley rats were exposed under identical conditions to those that resulted in induction of neoplasia in female rats of this strain (see preceding abstract), in an effort to assess the influence of male hormone on the neoplastic response of the breast tissue.

The male rats, both castrates and intact, had a 50 per cent incidence of breast neoplasms sixteen months after exposure to 400 r of 250-kvp total-body irradiation delivered as a single dose on the fortieth day. The dose was measured in air with scattering material in place. Nonexposed intact or castrate Sprague-Dawley male rats of the same age had an incidence of 0 or 6 per cent, respectively. In the time period studied, total-body irradiation induced more breast tumors than were found in nonirradiated rats, and after consideration of the report that nonexposed male rats of this strain allowed to live out their life span have an incidence of neoplasms of the breast that does not exceed 10 per cent, it is suggested that total-body irradiation can hasten onset of neoplasms and also induce a higher incidence of neoplasms of the breast of the male Sprague-Dawley rat.

As compared to the neoplastic response of the breast of the female Sprague-Dawley rat, the following differences were noted. The latent period between exposure and appearance of breast neoplasms was prolonged in the male; the total incidence of breast neoplasms was lower in the male; and more neoplasms of the male breast were classified as fibrosarcoma. From these findings, it is concluded that, although both male and female rats of the Sprague-Dawley strain respond to total-body irradiation by the formation of neoplasia of the breast, gonadal hormones can influence the frequency, latent period, and histological appearance of the induced tumors.

Five figures; 1 table.

The Response of the Kangaroo Rat (*Dipodomys merriami* Mearns) to Single Whole-Body X-Irradiation. Thomas J. Haley, R. G. Lindberg, A. M. Flesher, K. Raymond, W. McKibben, and Page Hayden. *Radiation Res.* 12: 103-111, January 1960. (University of California, School of Medicine, Los Angeles, Calif.)

The responses of the kangaroo rat (*Dipodomys merriami* Mearns) to single whole-body x-irradiation in the

dosage range 25 to 550 r have been studied. The ST 50 (survival time for 50 per cent) of this species at 550 r was 10.3 (9.7 to 10.9) days, which is almost identical to that of the CF-1 mouse. Observations were made of the following: total erythrocytes, total leukocytes, differential cell count, platelets, hemoglobin, hematocrit, bone marrow, and adrenal, kidney, spleen, and body weights. The responses of the kangaroo rat were essentially the same as those observed in the albino rat (see Lawrence *et al.* Radiology 51: 400, 1948), but the general symptomatology was different, reflecting, in part, the difference in intestinal flora. In the nonirradiated kangaroo rat, lymphocytes comprise 81.4 per cent of the total leukocytes and the spleen has an average weight of only 33 ± 2.88 mg.

Five graphs; 2 tables.

Effect of Homologous Bone Marrow-Spleen Cell Suspension on Survival of Swine Exposed to Radiation from a Nuclear Weapon. Harry W. Daniell and William H. Crosby. Blood 15: 856-862, June 1960. (Walter Reed Army Institute of Research, Washington, D. C.)

The authors have evaluated the effect of homologous marrow-spleen cell suspensions on survival of 69 swine exposed to mixed neutron and gamma irradiation from a nuclear weapon. The bone marrow-spleen mixture was administered to the animals by the intravenous, intracardiac, or intraperitoneal route. This treatment did not affect the survival of animals receiving sublethal, intermediate, or supralethal doses of irradiation. No evidence of accelerated repopulation of hematopoietic or lymphatic tissues was found in the treated animals that died, compared with untreated animals dying at the same time. Possible reasons for failure to demonstrate a beneficial effect on survival are discussed.

A unique method for recovery of bone marrow from the spine of mammals is described, with photographs showing the carpenter's plane used to gather the bone chips. The procedure for extricating the cells from the spleen is also described. The technic of homogenizing splenic tissue is illustrated.

Three photographs; 1 graph.

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Acceptance of Rat and Mouse Lung Grafts by Radiation Chimeras. George W. Santos, Richard M. Garver, and Leonard J. Cole. J. Nat. Cancer Inst. 24: 1367-1387, June 1960. (U. S. Naval Radiological Defense Laboratory, San Francisco, Calif.)

Rat-mouse bone-marrow chimeras, *i.e.*, lethally x-irradiated mice that had received injections of rat bone marrow, were given grafts of rat and mouse lung tissue by subcutaneous implantation at fourteen to two hundred and seventy days post-irradiation. The lung grafts were removed thirty-five to forty days after implantation, fixed in formalin, and the histologic sections examined microscopically for evidence of growth and persistence of the graft, or of its rejection.

In normal nonirradiated mice or in isologous chimeras (irradiated mice receiving injections of isologous

bone marrow), the mouse lung grafts grew well in 70 per cent of the recipients, while rat lung grafts were rejected in 100 per cent of the animals. In the heterologous chimeras given grafts at fourteen to thirty-eight days post-irradiation, rat lung tissue grew well in 50 per cent of the animals, while mouse lung tissue grew well in only 19 per cent (16 mice). In heterologous chimeras (19 mice) given grafts at fifty-five to two hundred and seventy days post-irradiation, rat lung grafts grew well in 58 per cent of the mice and mouse lung grafts in 69 per cent. These late chimeras appeared healthy and there was evidence of weight gain, growth of hair, and a return to normal lymphoid architecture. In 1 chimera, which lost its rat marrow graft at sixty days post-irradiation (as evidenced by the absence of alkaline-phosphatase-positive rat granulocytes in the peripheral blood), mouse lung tissue grew well, but rat lung tissue was rejected. On the basis of the present study, in the majority of long-lived heterologous chimeras, both rat and mouse cells exist or eventually exist in varying proportions in individual mice, which are capable of some immunological response in general, but incapable of reacting specifically to host or donor-type isoantigens.

Nine photomicrographs; 4 tables.

AUTHORS' SUMMARY

The Effects of X-Rays and Beta Rays (Tritium) on the Growth of Rickettsia mooseri and Rickettsia akari in Embryonate Eggs. Donald Greiff, E. L. Powers, Walter E. Kisieleski, and Henry Pinkerton. J. Exper. Med. 111: 841-849, June 1, 1960. (Marquette University School of Medicine, Milwaukee, Wisc.)

Changes were investigated in the growth patterns of *Rickettsia mooseri* and *Rickettsia akari* in embryonate eggs injected with a radiocompound as an internal source of continuous radiation. Alterations in the growth of *R. akari* in embryonate eggs receiving β -irradiation were also investigated. The radiocompound used was tritium-labeled water, which possesses unique advantages as an experimental source of ionizing radiation. It affords a uniform radiation field which can be introduced into any aqueous reaction system, and the short range of its beta particle simplifies calculations of dosimetry.

The growth of *Rickettsia mooseri* was accelerated and quantitatively increased in embryonate eggs containing tritium oxide at levels of 180, 90, and 45 mc/egg during the growth period. The eggs of a group containing 22.5 mc/egg showed only a slight increase in the rate of growth of organisms; the infections in the eggs of a group given 11.2 mc/egg did not differ significantly from those of the control group. On the other hand, growth of *R. akari* was inhibited in embryonate eggs containing tritium oxide at levels of 180, 90, and 45 mc/egg, and partially inhibited in groups containing 22.5 and 11.2 mc/egg. The patterns of growth of *R. mooseri* and of *R. akari* exposed to tritium oxide for six hours prior to inoculation into embryonate eggs did not differ significantly from those of the control group.

Single and divided doses of x-rays to the host resulted in partial inhibition of the growth of *R. akari*.

Six tables.

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